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RENAL FUNCTION AFTER SELECTIVE RENAL ANGIOGRAPHY

An experimental study in dogs

by

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In a previous experimental study (1958) the writers found that renal aortography with large doses of contrast medium after transfemoral catheterisation, performed in healthy dogs under general anaesthesia, did not cause failure in kidneys with intact functional capacity before the examination. The doses employed were approximately five times as high as those used in clinical aortography. We therefore presumed that properly performed aortographies after transfemoral catheterisation in man probably will not damage healthy kidneys.

This investigation led to a study of renal function also after selective renal angiography. However, since a systematic investigation of the risks attending selective renal angiography cannot be carried out in man, we have studied the response of the renal tissue to contrast medium injected directly into the renal artery in healthy dogs. In some animals renal

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function was tested by means of inulin and PAH (paraminohippuric acid) clearances and extraction ratios of PAH, before and after the injection of the contrast medium. In all the animals the kidneys were examined microscopically post-mortem. In addition, the angionephrographic effect (EDLING & HELANDER 1959) was compared with the functional and morphologic findings.

Methods

Before the injections of contrast medium, and the clearance determinations, the animals were lightly anaesthetized with a mebumal solution (pentobarbital + pentobarbital sodium + urethane) administered intravenously.

The contrast media (triiodine compounds: Miokon 30 % or 50 % and Rheopak 40 %; diiodine compound: Umbradil 35 % or 50 %) were injected into the renal arteries after catheterisation via the femoral artery as in man (EDHOLM & SELDINGER 1956). The tip of the catheter was positioned under fluoroscopy, with a small dose of the contrast medium, and placed about 1 to 2 cm into the artery. The main injection rate was about 5 ml per second. Exposures were made with a manual 4-film changer or an automatic film changer (GIDLUND 1956).

For determination of the functional capacity of individual kidneys 9 female dogs were operated upon. The left (in one the right) ureteral orifice with surrounding bladder wall was transplanted into the abdominal wall, and the left ovarian vein was ligated to prevent non-renal blood from entering the renal vein during the determination of the extraction ratio of PAH. For identification of the renal artery during fluoroscopy a silver ring of a diameter sufficiently large as not to cause compression, was in some experiments applied to the artery near its origin. The urinary flow, intravenous urography, and functional tests after the operations were normal, and post-mortem examinations of the urinary tract showed quite satisfactory healing.

A polythene catheter was passed up the femoral artery on one side and connected to a kymograph to register the blood pressure during the clearance determinations. In three animals, in which the blood pressure recording was started before the general anaesthesia, there were no significant variations of the pressure before and during anaesthesia. A radiopaque polythene catheter was passed up via the right renal vein for the determination of the PAH extraction ratio (HELANDER, ÅSHEIM and ÖDMAN 1958). Coagulation in the catheter was avoided by means of a slow continuous saline drip. The animals were hydrated with half a litre of water, through a gastric tube, an hour before the clearance periods started, to obtain diuresis during the examinations.

Inulin and PAH clearances were used as measures of glomerular filtration and effective renal plasma flow, respectively. After initial doses, inulin and PAH were administered intravenously by stabilized infusion to maintain an even plasma concentration of 15 to 25 mg per 100 ml of inulin and about 2 mg per 100 ml of PAH. Thirty to forty minutes after the infusion had started the clearance determinations were performed for 2 to 4 periods of 20 minutes' duration, blood being aspirated from the femoral artery and from the renal vein for determination of the extraction ratio of PAH in the middle of each period. Urine from the non-operated side was collected in the bladder after air filling and massage by means of a Foley catheter and from the operated side, without touching the transplanted ureteral opening, with the help of a specially constructed metal ring (HELANDER, ÅSHEIM & PERSSON 1958). Bladder urine was collected also by means of a Foley catheter in the dogs not operated upon.

Table

Comparison of angionephrographic, functional and morphologic findings in canine kidneys injected with contrast medium into the artery

Contrast medium	Dose in ml/kg body-weight	Interval between injection and sacrifice	Angionephrographic findings	Functional examination	Morphologic examination	
					Glomeruli	Tubules
Miokon 50%	1.4	4 days	+++	+++	+++	+++
	1.5	4 »	N	N	N	N
	1.5	4 »	+	+	+(+)	+(+)
	1.7	4 »	+++	+++	+++	+++
Miokon 30%	R 0.2	25 days	N	N	N	N
	L 0.2	25 »	N	N	N	N
	0.2	25 »	N	N	N	N
	0.3	25 »	N	N	N	N
	0.3	33 »	N	+	N	N
Miokon 50%	3.1	6 hours	+++	—	+++	+++
	1.9	12 »	+	—	++	++
	1.6	4 days	+++	—	+++	+++
	1.4	45 »	++(+)	—	+++	+++
	0.8	60 »	++	—	+	+
	1.3	66 »	+++	—	+++	+++
Miokon 30%	R 0.2	4 days	N	—	N	N
	L 0.2	4 »	N	—	N	+
	R 0.3	5 »	N	—	N	(+)
	L 0.3	5 »	N	—	N	(+)
	R 0.3	19 »	N	—	N	N
	L 0.3	19 »	N	—	N	N
Umbradil 50%	0.2	4 days	N	—	N	(+)
	R 0.4	5 »	N	—	++(+)	++(+)
	L 0.4	5 »	N	—	+	N
Umbradil 35%	0.2	17 days	N	—	N	N

R and L indicate that both kidneys were examined.
Normal findings denoted by N. Pathologic findings graded from (+) to +++.

Material

The material includes 24 healthy dogs of weights ranging from 9.5 to 27.5 kg; in all animals pre-examination of blood and urine showed normal values.

In 8 dogs injected with contrast medium (cf. the Table) both functional and morphologic examinations were performed. In all these animals inulin and PAH clearances were performed about one week before and three days after the injection of contrast medium; in one of the dogs a second clearance determination was carried out 13 days after the injection. In 7 animals the left ureter was transplanted and the injection made into the right renal artery; in the remaining dog, which was not operated upon, injections were made bilaterally. In four of the dogs operated upon, the dose of contrast medium was 1.4 to 1.7 ml Miokon 50 %/kg bodyweight; the morphologic examinations were performed four days after the angiography. In the four remaining dogs, the dose was 0.2 to 0.3 ml Miokon 30 %/kg bodyweight. This dose is approximately comparable with doses used up to now in man. The morphologic examinations were performed 25 to 33 days after the injection.

In 12 dogs (cf. the Table), morphologic examinations alone were made after the angiographies. In six of the dogs, 0.8 to 3.1 ml Miokon 50 %/kg bodyweight were injected into one renal artery and in three other dogs 0.2 to 0.3 ml Miokon 30 %/kg bodyweight in each of the both arteries. In the last three dogs Umbradil was injected: 0.2 and 0.4 ml of the 50 % compound/kg bodyweight in two of them, respectively, and 0.2 ml of the 35 % compound/kg bodyweight in one. The dose of 0.4 ml was injected in each artery. The dates for the morphologic examinations are also shown in the table.

In 2 more dogs a catheter of sufficiently heavy caliber to occlude the renal artery was intentionally used, the contrast medium thus being injected into ischaemic renal tissue. The catheter was not left in the artery for more than one minute. The doses of contrast medium were 0.5 ml Umbradil 50 %/kg bodyweight and 0.4 ml Rheopak 40 %/kg bodyweight, respectively. Morphologic examinations were performed after about four months.

In the remaining 2 dogs, in which one ureter was transplanted, 4.4 % hypertonic salt solution, representing the same osmotic pressure as a 50 % triiodine compound (Miokon), was injected into the renal artery. The dose was 1.6 and 1.7 ml/kg bodyweight, respectively, and the injection rate 8 to 10 ml per second. In these dogs the silver ring around the artery had been applied to enable positioning of the catheter in the artery. Clearance determinations were performed about one week before and three days after the injections, the morphologic examinations four days after the injections.

The sacrifice of all the dogs was followed by immediate laparatomy, the kidneys fixed in formalin and sections prepared for microscopic examination with haematoxylin-eosin and van Gieson stains.

Results

The clearance determinations in 10 of the dogs before the injection into the renal artery showed normal figures.

The results of the injections of contrast medium after ordinary angiography are brought together in the Table on p. 163 including contrast media, doses/kg bodyweight, times of sacrifice and a comparison of angionephrographic, functional, and morphologic observations.

Of the 4 first dogs, which received very large doses, three had an abnormal angionephrographic effect, disturbance of renal function, and

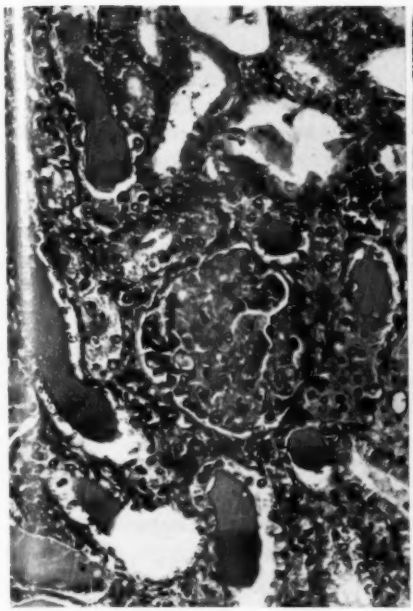

Fig. 1. Section from canine kidney 4 days after injection of 1.4 ml Miokon 50 % kg bodyweight into the artery. Necrotic glomeruli, dissolution of tubular cells, and hyaline casts in some of the tubules. Van Gieson.

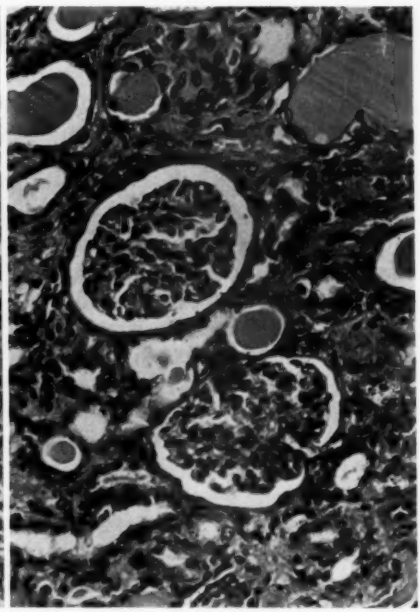

Fig. 2. Section from canine kidney 2 months after injection of 1.3 ml Miokon 50 %/kg body weight into the artery. Marked interstitial fibrosis and atrophic tubules with hyaline casts. Van Gieson.

morphologic changes in the injected kidney. Instead of a normal accumulation of contrast medium, the artery was contracted at the tip of the catheter, or contrast medium remained in the artery up to 35 seconds after the end of the injection; the increased density was irregular and occasionally remained for several minutes, and the renal vein was also filled for several minutes (EDLING & HELANDER 1959). Heller's test was also positive and red cells were found in the sediment. Macroscopically the injected kidneys were of normal size with infarctions surrounded by narrow haemorrhagic zones. Microscopically there were changes in both glomeruli and tubules, most severe in the superficial parts of the cortex. The glomeruli had focal hyalinization and dissolution of the convolutions. The tubular lesions were most marked in the proximal parts with granular necrosis in the epithelium; in some areas the tubules were dilated and contained exudate and numerous hyaline casts (Fig. 1). In the fourth dog the angionephrographic, functional and morphologic observations were normal, as were Heller's test and the sediment.

In three of the following 4 dogs, in which the smaller doses were injected, the angionephrographic, functional and morphologic conditions were normal after the injections. Heller's test was also normal. The fourth dog had transiently higher inulin clearance and a higher filtration fraction (C_{IN}/C_{PAH}) than normal, and Heller's test showed traces of proteinuria.

The next 6 dogs, which had received very large doses, all had an abnormal angionephrographic effect and morphologic changes. The angionephrographic findings were of the same type as described above. The morphologic changes in the two dogs sacrificed within 12 hours did not differ appreciably. They had reduced tingibility and nuclear pyknosis in both glomeruli and tubules. In the glomeruli the basement membranes were thickened and in some areas of the proximal tubules there were vacuolization or epithelial swelling; haemorrhages were present in the medulla. The dog sacrificed after four days had the same morphologic changes in the injected kidney as the two severely damaged dogs in the first group. The three remaining dogs were kept alive for one and a half to two months. The kidneys were of ordinary size; scattered depressions on their surface were observed and these by microscopy were found to be old infarctions. No lesions were observed in the glomeruli other than those in the fibrotic areas. Diffuse fibrous streaks extending from the papilla into the cortex contained atrophic tubules with hyaline casts (Fig. 2).

As to the last 6 dogs, which had received the smaller doses of contrast media, the angionephrograms were normal in all of them, and there were no or very little morphologic changes in 4. In one of the remaining two, in which 0.4 ml Umbradil 50 %/kg bodyweight was injected bilaterally, and which was sacrificed after five days, both the glomeruli and the tubules of the right kidney showed reduced tingibility with areas of granular necrosis; only occasional nephrons seemed to be intact. The left kidney had no tubular and much less advanced glomerular changes. In the last dog, in which 0.2 ml Miokon 50 %/kg bodyweight was also injected bilaterally and which was sacrificed after four days, the right kidney had no pathologic changes and the left a few small cortical areas with dilated tubules containing hyaline casts; the tubular epithelium in the proximal parts of these nephrons was atrophic.

The 2 dogs with occlusion of the renal artery during the injection of the contrast medium had advanced angionephrographic changes. On morphologic examination after about four months the kidneys into which the contrast medium had been injected were reduced to less than one-third of the normal size and the surfaces were of the type found in old infarctions. Microscopy showed cortical lesions with atrophy of large zones, hyalinized glomeruli, atrophic tubules, and in the remaining tubules numerous hyaline casts as well as marked interstitial fibrosis.

In the 2 dogs given injections of hypertonic salt solution there were

no disturbances of renal function. Morphologic examination of the kidneys showed no morbid changes.

In the kidneys of the dogs which received no injections there were no disturbances of function and/or no morphologic changes.

To summarize, it was found that in most cases injection of very large doses of contrast medium in selective renal angiography caused severe renal damage, demonstrable as an abnormal angionephrographic effect, most often greatly reduced renal function, and lesions in the glomeruli and the tubules, mainly of a degenerative character. This was confirmed by the presence of albumin and red cells in the urine. There was only an exceptional case in which the angionephrographic effect, the renal function, and the morphologic picture of the kidneys were normal. If the catheter occluded the renal artery during the injection of contrast medium, the renal damage was very severe.

It was further found that injection of doses of contrast medium approximately comparable with those used in selective renal angiography in man could cause a transient functional disturbance or lesions of the glomeruli and tubules, whereas, without exception, the angionephrographic effect was normal. After bilateral injection the morphologic changes might vary in severity in the two kidneys; in one animal the difference was marked.

After the injection of hypertonic salt solution into one renal artery no changes in the function or the morphologic appearances of the kidneys were observed.

The superficial anaesthesia used did not seem to be conducive to the renal injuries, in agreement with our experience in experimental aortography (1958). On the other hand, the anaesthesia did not impede vascular contractions.

Discussion

In the present material an abnormal angionephrographic effect was invariably associated with severe renal damage due to the injection of contrast medium. Hence, retention of contrast medium in the renal tissue indicated that the organ had been injured. A normal angionephrographic effect might be present in slight renal damage and exceptionally even in severe injury; it was always present in the absence of renal failure. Thus, the appearance of a normal angionephrographic effect does not exclude renal damage. The findings suggest, however, that a normal angionephrographic effect is usually not associated with any severe renal failure.

Idbohrn & Berg (1954) have pointed out that 'the absence of any

definite relationship between the severity of renal injury and the concentration argues against a direct toxic effect of the contrast medium on the epithelial cells and for a more complex cause'.

The present study yielded consistent results. Even if the largest doses, in high concentrations of the contrast medium, most often caused the most severe renal damage, there were clear exceptions. This suggests that factors other than the contrast medium as such may also have contributed to the damage. When present, the abnormal angionephrographic effect indicates a severe disturbance in renal circulation. However, in the presence of a normal angionephrographic effect the possibility cannot be ruled out that circulatory disturbances of less severity have occurred and are combining to produce renal damage. This ischaemia may be explained by irritation by the contrast medium. The observations in the cases in which the contrast medium was injected by means of a catheter occluding the artery, and in which the renal damage was very severe and extensive, also suggest the importance of ischaemia. Moreover, FAJERS (1956) found that cholaemia will produce a more marked nephrosis if the kidney has suffered even a brief ischaemia. Ischaemic renal tissue is therefore probably more susceptible to injury than normally vascularized tissue.

The kidneys are highly vascularized organs and adapted to great variations in the blood flow. If therefore a substance is injected into the renal artery, its concentration and duration of contact with the renal tissue will be dependent on the blood flow at the moment of injection. It has been shown (HELANDER, PERSSON & ÅSHEIM 1958) that the very introduction of the catheter sometimes causes a disturbance in renal function. Thus, even the catheterisation itself may involve the risk of ischaemia.

The concentration of the contrast medium after injection will be higher in a reduced than in a normal blood flow, and the amount of the substance acting per unit of tissue will be greater. The reduction in the glomerular filtration also has the effect that some amount of the contrast medium that would normally be filtered, is instead retained in the blood and reaches the tubular cells. This may explain the variable correlation obtained between the renal damage and the amount and concentration of the contrast medium injected. It seems that there are greater risks of causing damage to the kidney in selective renal angiography than in renal aortography.

SUMMARY

Selective renal angiography after femoral catheterisation has been performed experimentally in healthy dogs. Renal injury usually follows injection of large doses of contrast media but in some cases there is no invariable correlation between the degree of

verity of the damage and the dose and the concentration. Ischaemia of the renal tissue ems to be of importance. The study suggests that the risks of renal damage are greater in lective renal angiography than in renal aortography.

ZUSAMMENFASSUNG

Selektive renale Angiographien nach Femoraliskatheterisierung sind bei gesunden unden durchgeführt worden. Eine Nierenschädigung erfolgte gewöhnlich nach Injection osser Dosen des Kontrastmittels. In einingen Fällen lag jedoch keine konstante Korrelaon zwischen der Schwere des Nierenschadens und der Dosis und Konzentration des ontrastmittels vor. Ischämie des Nierengewebes scheint von Bedeutung zu sein. Die ntersuchung legt dar, dass das Risiko einer Nierenschädigung bei der selektiven renalen giographie grösser ist als bei der renalen Aortographie.

RÉSUMÉ

Les auteurs ont fait sur des chiens en bonne santé des angiographies rénales sélectives expérimentales par cathétérisme de l'artère fémorale. Habituellement l'injection de grandes quantités de moyen de contraste est suivie de lésion rénale, mais dans certains cas il n'y a pas de relation constante entre la gravité de la lésion rénale et la dose ou la concentration du moyen de contraste. L'ischémie rénale semble jouer un rôle important. Ce travail fait penser que les dangers de lésion rénale sont plus grands avec l'angiographie rénale sélective qu' avec l'aortographie rénale.

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GASTROGRAFIN AS WATER SOLUBLE CONTRAST MEDIUM IN ROENTGEN EXAMINATION OF THE G. I. TRACT

by

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Barium sulfate suspended in water is, at present, the contrast medium of choice in roentgen examination of the gastrointestinal tract, despite several known disadvantages. Modification of the basic formula by the use of micronized particles of barium sulfate and the addition of suspending agents such as tragacanth and carboxymenthylcellulose has been advocated by some radiologists. In any regime using barium sulfate, however, the following difficulties are encountered due to factors inherent in the nature of the medium itself. As the barium particles sediment from suspension and the opacity of the medium undergoes change, pathologic changes within the excessive opacity of the sediment or within the lesser opacity above may escape detection. In the presence of excessive mucus, the barium particles tend to form aggregates and clump. For reasons as yet poorly understood, the barium particles are sometimes capricious as to their adherence to the underlying mucosa. The particulate nature of the barium suspension and its immiscibility with blood makes the detection of bleeding points difficult.

Although the use of barium sulfate as a contrast medium is usually innocuous, undesirable sequelae are known to occur. Barium will inspissate

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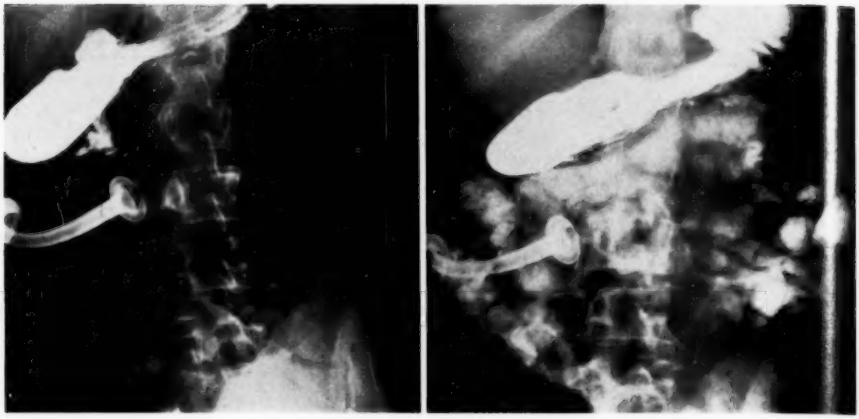
Fig. 1. Large bleeding antral ulcer of the greater curvature, histologically benign, after 30 ml Gastrografin.

following prolonged retention within the bowel due to absorption of the suspending water. Granulomata may occur following leakage of barium into body cavities or following retention within fistulous tracts. Necrotizing bronchopneumonia has been reported following accidental aspiration.

In the hope of overcoming some of these disadvantages, attention has been directed to the use of water soluble contrast media. The aqueous organic iodides have received widespread acceptance as contrast media for use in pyelography and angiography but little use has been made of them in roentgen examination of the gastrointestinal tract. They have been reported in human and animal experiments to be relatively non-absorbable and therefore non-toxic when administered into the lumen of the gastrointestinal tract. These media are true solutions with low viscosity as compared to barium, and being solutions will not sediment. They are miscible with blood and body fluid.

The recent literature, however, contains several reports by independent investigators who have evaluated the use of these media in roentgen examination of the gastrointestinal tract. A summation of these independent reports has not yet been published and should be of value to the radiologist in a total analysis of these media and their potential application.



a b

Fig. 2. a) Barium filled stomach and proximal duodenum after 4 hr 30 min in clinically suspected small bowel obstruction. b) One hour after administration of Gastrografin: contrast medium in ileum. No evidence of obstruction.

An independent study of one of these contrast media (Squibb Gastrografin 76 %) has been conducted for the past 8 months in the roentgen department of the Roswell Park Memorial Institute. An analysis of the results of this study and of the published results of other investigators to date is the subject of this article.

Material and Method

We have used Gastrografin 76 % (Squibb), a palatable, lemon-flavoured preparation identical, except for the added flavouring, with Renografin, the 76 % Squibb medium for intravenous urography. The additional flavouring disguises the bitter taste which has usually forced previous investigators to administer the media through a nasogastric tube. Gastrografin 76 % is an aqueous solution of sodium and methyl glucamine salts of renographic acid. The 76 % solution contains 59.7 % of renographic acid and 37 % iodine. The solution is hypertonic as compared to the intestinal and gastric secretions and has the advantages of low viscosity and miscibility with blood and body fluids.

The initial phase of the study comprised examination of the gastrointestinal tract of 40 patients using Gastrografin as the sole contrast medium. All patients were adults and were selected only in so far as those with a known sensitivity to iodides were excluded. Selection was also

Fig. 3. Obstructing colon lesion in distal sigmoid. Despite obstruction, the proximal colon is well filled.

Fig. 4. Normal mucosa of stomach after 15 ml Gastrografin.

directed towards those patients presenting a diagnostic problem in which it was hoped that the physical properties of this medium might prove helpful in arriving at a diagnosis. Oral use of this medium was pursued in cases of suspected tracheoesophageal fistula, to locate a bleeding focus in the gastrointestinal tract (Fig. 1), in suspected bowel obstruction (Fig. 2) and in the presence of bowel fistula. Gastrografin enemas were used in obstructive lesions of the colon in an attempt to delineate the proximal extent of the obstructing lesion (Fig. 3), in a study of defunctioned segments of the colon and also in a search for colonic polyps. It was also administered by injection into fistulous tracts. In several cases, examination with Gastrografin followed within 1 to 7 days of a previous examination with barium affording a possibility of comparative evaluation of both contrast media. It was established early that concentrations of Gastrografin less than 76 % were not satisfactory for detailed study and in almost all cases the concentration and amount used in the study of the upper gastrointestinal tract was 30 to 60 ml of Gastrografin 76 %. In enema studies, 240 ml of Renografin 76 % was used which was occasionally diluted to 480 ml of Gastrografin 38 % in those cases where the smaller amount of contrast medium was considered insufficient for a complete examination.

Table 1

Investigator	Material used	Concentration	Amount	No. of cases	Absorption reported	Advantages	Disadvantages	Side effects
DAVIS et coll.	Urokon Sodium Hypaque	Adults: 35 to 70% Children: 50%, or less	25 to 50 ml	Not stated	"Absorbed in minimal amounts"	1. Better delineation of gastric mucosa 2. Small duodenal ulcers demonstrated in several cases 3. Better filling of fistulas and stenotic bowel segments	High price	Slight diarrhoea
CANADA, W. J.	Urokon	15% to 70% Concentrations less than 30% are not satisfactory	50 to 150 ml	13	Absorption reported in 4 cases	1. Disappeared rapidly from abscesses and fistulous cavities 2. Requirements for fluoroscopic visibility were satisfactorily met 3. Indications for use a. Defunctioned bowel b. Fistula and abscess cavities c. Perforation d. Ulcerative colitis	Mucosal coating not as satisfactory as with a suspension	None noted in this series
EFSTEIN, B. S.	Hypaque Renografin	30 to 90% Good results in 50 to 90% concentration	Not stated		No absorption reported	In cases of suspected small bowel obstruction, mucosal pattern of stomach and duodenum and proximal 1/3 of the jejunum reported good	Mucosal pattern of distal 2/3 of jejunum and ileum reported often indistinct	None noted

Discussion

The aqueous organic iodides have been evaluated by several previous investigators and their published results are summarized in Table 1. The results in our series of 40 cases using Gastrografin as the contrast medium are as follows.

Taste was acceptable to the patient in all cases. The mucosal relief of the gastric rugae manifested a fine and delicate pattern (Fig. 4) but occasionally 'skip' areas resulted from lack of adherence of the contrast medium to the gastric mucosa. It is probable that the particulate nature of a suspension is more satisfactory than a solution for mucosal studies.

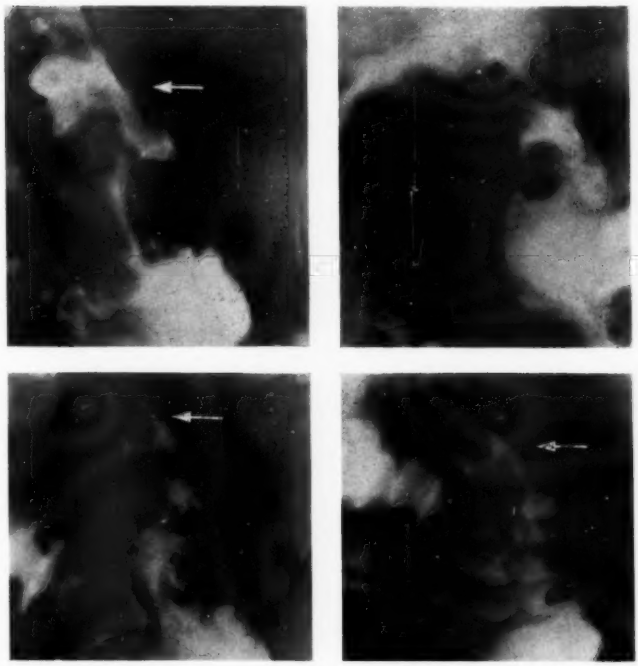


Fig. 5. Deformed duodenal bulb with small ulcer.

However, in several cases with gastric hypersecretion and excessive mucus formation, barium studies were unsatisfactory due to rapid sedimentation and clumping of the barium particles. Follow-up studies with Gastrografin in these cases were a definite aid to diagnosis. The medium passes quickly through the stomach, requiring rapid fluoroscopic examinations but facilitating the study of those cases with pyloric stenosis in which barium passage through the stenotic segment is delayed. In cases of pyloric stenosis, Gastrografin is the medium of choice. In one case of suspected duodenal ulcer in which careful fluoroscopic examination with barium elicited a deformed duodenal bulb but no evidence of a duodenal ulcer, a repeat study the following day with Gastrografin showed definite evidence of a small area of ulceration within the duodenal bulb which had not been detected on the previous barium study (Fig. 5). Also in cases of tracheoesophageal fistulae or other pathologic changes in which aspiration of barium is anticipated, Gastrografin is the medium of choice and we have found it superior to Lipiodol which has an oil base and therefore has a tendency for globlet formation.

Fig. 6. Normal small bowel. Cecum filled after 45 min.

Gastrografin being a hypertonic solution becomes rapidly diluted in the small bowel as a result of extravasation of fluid from the bowel mucosa. The filling of the small bowel distal to the 2nd portion of the duodenum was not quite sufficient for detailed morphological study but adequate for detection of obstructive lesions and bowel fistulae. Passage of Gastrografin through the small bowel is rapid with filling of the cecum at 45 minutes in almost all cases (Fig. 6). In our experience, failure of Gastrografin to reach the cecum within three hours is indicative of small bowel obstruction. In the colon, the density of the Gastrografin increases as a result of fluid absorption and although in our study no pathologic changes in the large bowel were detected on the basis of oral administration of Gastrografin solution, EPSTEIN (1957) reports two cases of carcinoma of the cecum detected following oral administration of an aqueous organic iodide contrast medium. In four cases, we performed air contrast studies with Gastrografin in an attempt to detect colonic polyps, but the examinations were not considered superior to conventional air barium studies.

Following completion of the initial phase of our study, the use of a combined medium of barium sulfate and Gastrografin was suggested by one of us (R. M. L.) in the hope of combining the good mucosal detail of the barium suspension with the advantages of low viscosity, homogeneity and miscibility with blood and body fluids of the Gastrografin solution. The combined contrast medium was prepared by the addition of 40 ml of Renografin 76 % to each quart of the conventional barium-water suspension. As utilized in 35 consecutive examinations of the gastrointestinal tract, studies of excellent technical quality were obtained in all cases. This combined medium is undergoing further evaluation in our department.

Comment

No toxic effects were noted in any of the cases of our series and no side effects other than diarrhoea have been reported in the literature. No gross absorption of contrast medium was noted in our study, but it would require marked and rapid absorption to be radiographically detectable. CANADA (1955) in a study of the gastrointestinal tract, using Urokon in 13 cases, reported gross absorption as evidenced by the appearance of pyelograms in four of these cases. There is little question but that some absorption of these contrast media does occur and the term 'non-absorbable' which has been applied to these media is an unfortunate one and can lead to a false sense of security.

These media being hypertonic are similar in action to saline cathartics and in our opinion their oral use is contraindicated in any condition in which the use of a cathartic is likewise contraindicated. We would consider their use hazardous in any case in which the possibility of acute appendicitis or of complete mechanical bowel obstruction enters into the differential diagnosis.

SUMMARY

Gastrografin 76 %, an organic iodide in a palatable aqueous solution, was evaluated as the sole contrast medium in radiography of the gastrointestinal tract of 40 patients. Mucosal detail was not as well demonstrated with Gastrografin as with barium sulfate, possibly because a suspension is superior to a solution for mucosal studies. It is the medium of choice when prolonged retention of contrast medium within fistulous tracts, body cavities or bowel lumen is anticipated and in those conditions where the possibility of aspiration of contrast medium may occur. An additional 35 patients were examined by a combined medium of diluted Gastrografin and barium in a preliminary investigation which indicated that this combined medium deserves further evaluation. Suggested contraindications to the use of aqueous organic iodide in radiography of the gastrointestinal tract are iodide sensitivity, acute appendicitis and complete mechanical bowel obstruction.

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ZUSAMMENFASSUNG

Das 76 % Gastrografin, ein organisches Jodid in einer wohlschmeckenden wässerigen Lösung, wurde als einziges Kontrastmittel bei der Röntgenuntersuchung des Magen-Darmkanales von 40 Patienten bewertet. Schleimhauteinzelheiten wurden mit Gastrografin nicht so gut dargestellt wie mit Bariumsulfat; möglicherweise beruht dies darauf, dass eine Suspension einer Lösung für Schleimhautstudien überlegen ist. Es ist das Mittel der Wahl, wenn Retention des Kontrastmittels in Fistelgängen, Körperhöhlen oder Darmlumen erwartet wird sowie bei denjenigen Zuständen, wo die Möglichkeit der Aspiration des Kontrastmittels eintreffen kann. Weitere 35 Patienten wurden mit einer Kombination aus schwächerem Gastrografin und Barium präliminär untersucht. Hierbei ergab sich, dass das kombinierte Kontrastmittel noch weiterer Prüfung würdig ist. Kontraindikationen für die Benutzung wasserlöslicher organischen Jodide bei der Röntgenuntersuchung des Magen-Darmkanales sind Jodüberempfindlichkeit, Appendicitis acuta und völliger mechanischer Darmverschluss.

RÉSUMÉ

La Gastrografin 76 %, sel organique d'iode en solution aqueuse de goût agréable, a été utilisée à titre d'essai comme seul moyen de contraste en radiographie du tube digestif chez 40 malades. La Gastrografin n'a pas aussi bien mis en évidence les détails de la muqueuse que le sulfate de baryum, peut-être parce qu'une suspension est supérieure à une solution pour l'étude de la muqueuse. Elle est le produit de choix quand on prévoit une rétention prolongée du moyen de contraste dans des trajets fistuleux, des cavités du corps ou la lumière intestinale, et dans les cas où l'aspiration du moyen de contraste peut se produire. 35 autres malades ont été examinés, dans un travail préliminaire, avec un mélange de Gastrografin diluée et de baryum; il en résulte que ce moyen de contraste mélangé mérite une étude plus complète. Les contre-indications possibles à l'emploi d'iode organique en solution aqueuse pour la radiographie du tube digestif sont la sensibilisation à l'iode, l'appendicite aigüe et l'occlusion intestinale mécanique complète.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: HELGE CHRISTENSEN), ROSKILDE AMTS OG BYS SYGEHUS, ROSKILDE, DENMARK

RETROCAVAL URETER

Report of a case

by

P. Birger Nielsen

Retrocaval ureter is a rare anomaly due to an abnormal development of the inferior vena cava in foetal life and can be diagnosed preoperatively only by roentgen examination. The ureter has at first a spiral course behind and medial to the vein, and then runs in the normal way forwards and downwards to the bladder. This anomaly is also called postcaval ureter, circumcaval ureter, deflected ureter or preureteric vena cava inferior, the last mentioned name being aetiologically the most correct one. The clinical importance of the condition lies in the hydronephrosis which gradually appears due to compression of the ureter between the vena cava and the lumbar spine. The only treatment is operative, with surgical correction of the renal pelvis, ureter, or inferior vena cava. Since surgical repair has to be performed before the renal function has become too far compromised, and since, as pointed out by PICK & ANSON, the abnormal course of the ureter may be overlooked in an operation by the ordinary lumbar approach, a correct preoperative diagnosis is of the utmost importance. This anomaly should be borne in mind in any case of hydronephrosis of obscure origin.

Retrocaval ureter was described for the first time by HOCHSTETTER in 1893. The only Scandinavian case is GREGERSEN's of 1946. A total of 83 cases have been reported, including the present one. In post-mortem series the incidence has been found to be 0.9 cases per 1,000, a high rate

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considering the number of published cases. The only explanation is unfamiliarity with the typical anomaly; an increasing number of cases has been published during the past few decades. In 1940 the first preoperative diagnosis was made (HARRILL). During the period 1893 to 1939 only 27 cases were reported, while in the 1940—1956 period 61 cases were published, 41 of these within the past 7 years. A preoperative diagnosis was made with increasing frequency: in the decade 1940—1949 in 10 out of 17 operated cases, and during the period 1950—1956 in 20 out of 23 operated cases.

All the roentgenographic findings have been typical or so suggestive as to indicate further investigations. Thirty-seven cases were diagnosed by urography whereas in 17 cases the diagnosis was not made until the operation, despite typical or extremely suggestive roentgenographic appearances. In one case post-mortem pyelography showed characteristic features. The first case examined by urography was published in 1935 (KIMBROUGH).

Out of the 75 cases in which the sex is stated 55 were males and 20 females, *i. e.* a ratio of 2.8/1, a significant, but unexplained male preponderance. The average age is 35.1 years in 70 cases in which the age is known. The condition frequently remains asymptomatic for many years, and as a rule symptoms do not appear until the 3rd or 4th decade. The age distribution is given in the Table below which shows that 41 out of 70 patients were in the 21 to 50 year range. Both the youngest and the oldest cases, a still-born acardiac infant and a male of 84 years, were reported by GLADSTONE (both were autopsy cases).

Table

Age distribution in 88 published cases

Age in years	Number of cases	
0—10	6	
11—20	9	
21—30	14	
31—40	15	
41—50	12	
51—60	9	
61—70	2	
71—80	2	
81—90	1	
Adults		6
Age not stated		12
	Total:	70 + 18

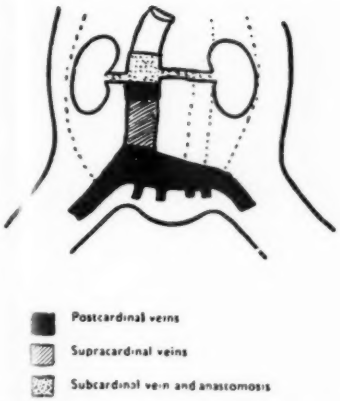


Fig. 1. Embryologic components of the inferior vena cava (after YOUNG).

Embryology and types. The reader who is particularly interested in the embryology is referred to MCCLURE & BUTLER and to PICK & ANSON. Certain details will, however, be mentioned.

In foetal life there are in the abdomen three longitudinal paired venous channels which anastomose to form the periureteric ring or, as HUNTINGTON & MCCLURE call it, 'the renal collar'. This ring which contains centrally the permanent kidney, the metanephros, is made up of the following vessels: ventrally and laterally (1) the post-cardinal veins which form, together with the anterior cardinal veins (of no significance in this connection), the canal of Cuvier, a tributary of the sinus venosus, ventrally and medially (2) the subcardinal veins and dorsally and laterally (3) the supracardinal veins on either side of the aorta and the sympathetic trunk. Of the above-mentioned vessels the postcardinal veins on the left disappear entirely, whereas the right develop into the azygos vein. The subcardinal veins and their anastomoses become the internal spermatic veins, the upper parts on the right side become the suprarenal segment of the inferior vena cava, the right renal vein, and the right suprarenal vein, while the upper parts on the left side become the left renal vein and the left suprarenal vein (Fig. 1). As regards the supracardinal veins, the left disappears, whereas the normal inferior vena cava develops from the right. Through this ring of veins and anastomoses the kidneys and ureters ascend to reach the renal fossa in the 5th foetal month. Since the right supracardinal vein, which is situated dorsally, becomes the normal inferior vena cava, the ureter becomes precaval. Disturbances in the normal development of the veins may produce a postcaval course of the ureter. There are various possibilities: the postcardinal vein may persist, while the supracardinal vein, which ought to persist, disappears; the supracardinal vein may not develop, the postcardinal vein forming the inferior vena cava; the postcardinal as well as the supracardinal vein persist, the ureter passing between two inferior venae cavae, an anterior and a posterior limb. Since developmental disturbances may occur both on the right and on the left side, there are many possibilities of variations.

According to HUNTINGTON & MCCLURE there is a theoretical possibility of 15 different forms of preureteric inferior vena cava, 12 of which have been observed in animals. Five different variations have so far been described in man, as follows:

Group I, (Fig. 2 a), 59 out of 71 cases. Unilateral right-sided single preureteric vena cava. Persistence of the right postcardinal vein, disappearance or failure of development of the right supracardinal vein.

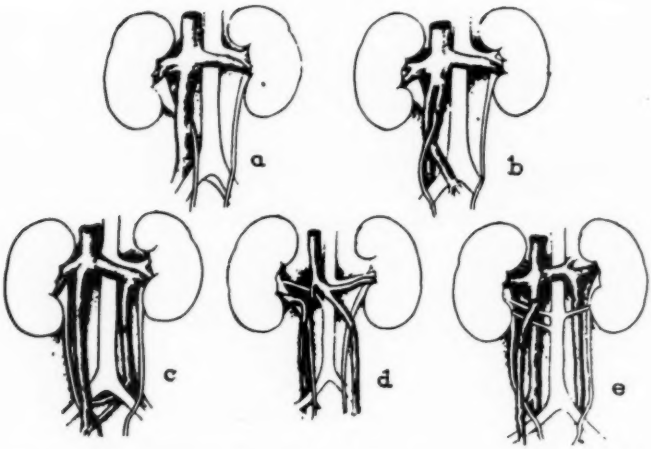


Fig. 2. Graphic representation of the 5 types of retrocaval ureter found in man (after GOYANNA).

Group II, (Fig. 2 b), 4 cases. Unilateral right-sided double inferior vena cava. Ureter between the two veins. Persistence of the right supracardinal vein and of the right postcardinal vein.

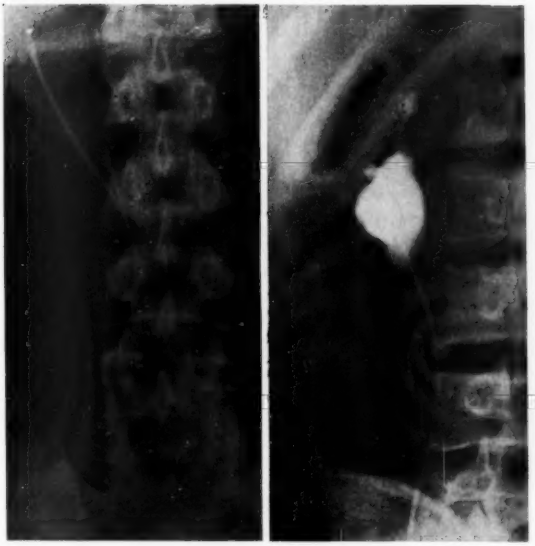
Group III, (Fig. 2 c), 6 cases. Bilateral, single inferior vena cava, the right being preureteric and the left postureteric. Persistence of the right postcardinal vein and the left supracardinal vein.

Group IV, (Fig. 2 d), 1 case (GLADSTONE's). Bilateral single preureteric inferior vena cava. Persistence of the right and left postcardinal veins.

Group V, (Fig. 2 e), 1 case (GRUENWALD & SURK's). Double right vena cava, ureter between the two veins, single postureteric left vena cava. Persistence of the right supracardinal and postcardinal veins as well as of the left supracardinal vein.

In addition to the 71 cases already mentioned, a further 17 are on record, but the latter cannot be classified, as no post-mortem or operative findings are available.

Clinical features. There are no pathognomonic signs of retrocaval ureter. The symptoms are due exclusively to the obstruction and are thus similar to those caused by hydronephrosis of a different aetiology; since the development of the hydronephrosis is slow, the symptoms do not appear until relatively late. In 70 cases of known age only 15 were under 20 (cf. the Table). As in all cases of hydronephrosis, infection is a common complication, and calculi may occur.



a b

Fig. 3. a) Supine position. Radiopaque catheter introduced into the right ureter shows typical medial displacement. b) Oblique view. Catheter in the right ureter which runs dorsally towards the vertebral column.

Diagnosis

The diagnostic methods are excretory urography, the introduction of a radiopaque catheter into the ureter, retrograde pyelography, or venography combined with these methods. Anteroposterior, oblique and lateral views should always be obtained. LEBERMAN & ZINSSER (1952) showed in the cadaver that the retrocaval ureter may be demonstrated by a radiopaque catheter introduced into the inferior vena cava combined with pyelography. In 1956 PRESMAN & FIRFER diagnosed a case by retrograde pyelography in which, at the same time, they introduced a radiopaque catheter into the inferior vena cava through the great saphenous vein. These authors claim that this method is technically easy, involves little risk of thrombosis, and that, unlike combined venography and pyelography, it need not be performed in a hurry.

The following changes are typical of retrocaval ureter:

1. In long-standing cases, hydronephrosis with hydroureter in its upper course proximal to the site of crossing. The remaining part of the ureter has a normal calibre.

2. Medial displacement of the ureter at the level of the 3rd and 4th lumbar vertebrae. The ureter may frequently be projected close to the spinous processes. In none of the ordinary type of cases (single right-sided preureteric vena cava) has the ureter been lateral to the lumbar pedicles. In cases of a double unilateral vena cava the ureter may be seen on a level with the transverse processes, since at this site the calibre of the vessels is smaller.

Fig. 4. A. p. view in upright position, 2 hours after retrograde pyelography. Typical S-configuration with hydronephrosis and elongation of the pelvis and proximal ureter, as well as retention.

3. In the lateral and oblique views the ureter is seen to run, as first pointed out by RANDALL & CAMPBELL in 1935, dorsal and medial towards and close to the vertebral column. In cases of a unilateral double vena cava this is less evident owing to the interposed dorsal vein.

4. In the presence of more marked hydronephrosis the pelvis and the ureter are elongated, presenting a typical S-shaped configuration.

5. At urography no filling of the ureter distal to the site where it is crossed by the inferior vena cava is obtained.

6. The ureter pursues a spiral course.

7. Venography combined with excretory urography, retrograde pyelography, or the passage of a radiopaque ureteral catheter shows the exact course of the inferior vena cava encircled dorsally and medially by the ureter and discloses a double vein, if any. A bilateral vena cava may only be ascertained preoperatively by injecting contrast medium into both the right and the left femoral veins.

Differential diagnosis. It is generally not difficult to differentiate the condition from hydronephrosis due to other causes. Dilatation of the internal spermatic vein may produce a defect in the contrast-filled ureter, but this defect is too small to represent the inferior vena cava, and the

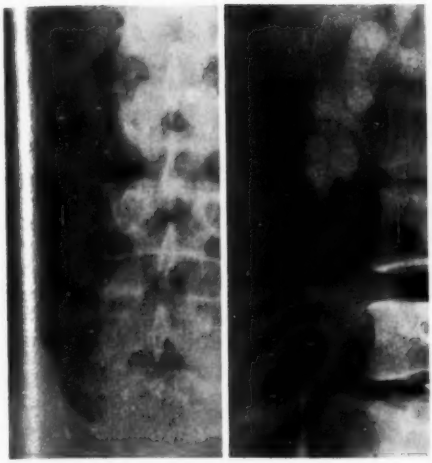


Fig. 5. Same case as in figs. 3 and 4, two months after operation. Catheter in the right ureter, the position of which is normal.

S-shape is not marked. In the presence of a double vena cava on the right or left side the calibre of the preureteric vessel may, however, be considerably smaller than normal. The course of the ureter in the lateral and oblique views is decisive. No confusion ought to arise by reason of an arcuate course of the ureter over an unduly prominent psoas major. In such cases, the arch will be straightened out when the catheter is introduced; there is no medial displacement and no hydronephrosis, and the ureter has a normal, slightly ventral curve away from the spine.

Treatment. Asymptomatic cases with no or only slight hydronephrosis should merely be kept under observation and subjected to regular urographic examinations so that any possible increasing ureteral obstruction may not escape detection. The treatment is otherwise purely surgical, *i. e.* nephrectomy in cases with seriously compromised function, or plastic repair of the pelvis or ureter if the renal function is still sufficient. In the latter case the pelvis or ureter is divided and the retrocaval segment freed and re-anastomosed in a pre-caval position. In cases of severe changes in the ureteral structure, the post-caval segment may be resected; the results are generally good.

In one case LOWSLEY tried to divide the ureter at the ureterovesical junction and to free and re-implant it in an antecaval position into the bladder, but without success.

A third method, tried by CATHRO in 1952, is ligation and section of the inferior vena cava distal to the renal vein. His patient developed postoperative paralytic ileus, oedema of both lower limbs, and thrombophlebitis of the right great saphenous vein. The end-result was, however, good; the hydronephrosis subsided, and there were no further signs of circulatory disturbances. This daring intervention seems particularly indicated in cases of bilateral inferior vena cava or double unilateral vein. CATHRO also suggests the possibility of section and re-anastomosis of the inferior vena cava into a normal post-ureteric position after freeing the ureter. This eliminates the risk of postoperative ureteral stricture. In CATHRO's opinion, this operation is indicated in those cases in which the freed postcaval ureteral segment is grossly normal, without strictures, and exhibits normal peristalsis. For further details of the surgery the reader is referred to ABESHOUSE & TANKIN.

Case report

Male, aged 22 years, with frequency of a few years duration. There had been no other urinary symptoms and no low-back pain. Before admission he suddenly developed severe non-radiating, and at times colicky, pain in the region of the right kidney. The pain rapidly subsided under morphia, but a few hours later the patient had severe haematuria.

Urography revealed right-sided hydronephrosis with somewhat delayed excretion; the cause was not evident. *Pyelography* showed a typical retrocaval ureter. The catheter proved to be medial to the lumbar pedicles and, in an oblique view, just anterior to the vertebral column (Fig. 3); the pelvis and upper part of the ureter were dilated and S-shaped, the ureter winding in the typical spiral course around the anteriorly situated vena cava (Fig. 4). There was prolonged retention; the renal pelvis still contained contrast medium after 4 to 5 hours.

One week later a plastic operation by the HARRILL method was performed on the right ureter. The operative findings confirmed the pyelographic diagnosis. The ureter wound medially behind the inferior vena cava, appearing again on the medial side of the vein further down. No origin of the left common iliac vein could be seen. The case thus belonged to the afore-mentioned Group III — persistence of the right post-cardinal vein and the left supracardinal vein. The ureter was freed, and the pelvis divided and re-anastomosed in an antecaval position. After this procedure, filling of the ureter and ureter peristalsis were evident. The postoperative course was uneventful. Follow-up urography showed decreasing dilatation and a normal position of the ureter (Fig. 5).

SUMMARY

A case of retrocaval ureter with successful surgical repair is presented. The aetiologic, clinical, and diagnostic factors are discussed and the literature on previously published cases is reviewed.

ZUSAMMENFASSUNG

Ein Fall mit retrocavalem Ureter, der chirurgisch erfolgreich behandelt wurde, wird vorgelegt. Die ätiologischen, klinischen und diagnostischen Faktoren werden diskutiert und die Literatur über bisher veröffentlichte Fälle wird kritisch behandelt.

RÉSUMÉ

Présentation d'un cas d'uretère rétro-cave traité chirurgicalement avec succès. L'auteur étudie les facteurs étiologiques, cliniques et diagnostiques et passe en revue les cas publiés auparavant.

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APPARATUS FOR THE DIRECT TIME MARKING OF SERIAL FILMS

by

Kjell Liverud

In rapid serial roentgenography, in which exposures are made at short and sometimes varying intervals, it is important to know the exact time at which each individual film was exposed. This is especially true in angiocardiographic investigations where the time of each single exposure in relation to the movements of the heart should be recorded.

The exposures and the time of injection of the contrast medium are ordinarily registered by connecting the equipment with an electrocardiograph through an elaborate and necessarily expensive apparatus. The individual films are then timed on the basis of the ECG, and the time is written in ink or crayon on each. If the series is made upon cut film, as distinct from roll film, an error in the numbering may produce erroneous timing. Moreover, the writing may be rubbed off in the course of time and if the ECG has been lost it may be difficult to reconstruct the film series. Serial roentgenography may even be performed without a film changer, without a program selector, or without an apparatus for timing the exposures, and in these cases the timing will be based largely on assumption or subjective judgment.

I have long felt the need for an automatic and reliable timing method for each individual film in serial roentgenography. For ordinary aorto-

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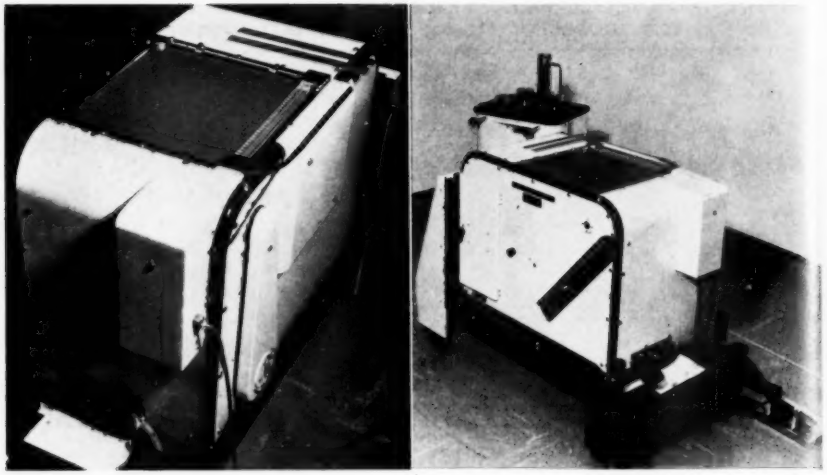

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Fig. 1. a) Scale with time marker mounted on one side of exposure field of film changer. The box in front (with cable) houses the electric motor and clutch. The two aluminium plates will, if necessary, prevent over-exposure of the scale. b) The marker is connected with the automatic high pressure injection syringe and the 'clock' is started by the same impulse that commences the contrast medium injection.

grams, venograms, etc., where the time of exposure in relation to the phase of the heart action is not so important, we have constructed a simple apparatus which fills our requirements completely. The apparatus was designed and constructed in the physics laboratory of the hospital by one of our technicians (SOLVANG).

A strip of perspex, about 30 cm in length, is placed along one side of the photographic field and forms a scale on which intervals are marked by grooves filled with red lead. A roentgen opaque time marker runs along the scale and is held taut by springs (Fig. 1 a). The marker is driven by an electric motor and moves from 0 to 30 at a rate which is adjusted so that each interval on the scale, about 1 cm, corresponds to 1 second. In order to ensure smoothness of movement, the motor is started first, and at a given time the marker is connected by means of a clutch. The scale and marker are exposed on each film as it is exposed. When the marker has run through the entire scale of 30 seconds it returns automatically to 0.

We almost always take serial roentgenograms in our department with the Schönander film changer for cut films (not roll films) and the injection of contrast medium is made with Gidlund's automatic high pressure syringe (Elema). We have therefore found it practical to mount the

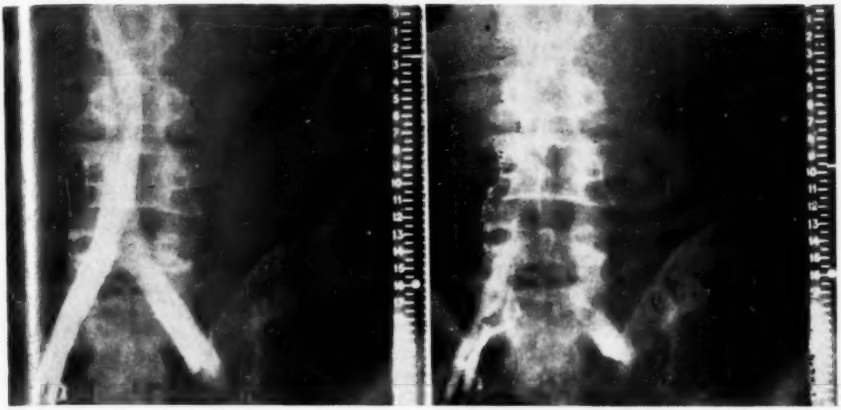

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Fig. 2. a) Examination of vena cava in a case of malignant carcinoidosis. The film was exposed, as shown by the scale, 2.5 sec after the beginning of the contrast injection. b) Retention of contrast medium in pelvic veins 9.5 sec after injection.

'clock' on the film changer. This must be done in such a manner as not to interfere with any servicing which may be required to the film changer. (Fig. 1 b.) The electric motor is started by the same impulse which prepares the Gidlund syringe for use, and the clutch is released by the same impulse which commences the actual injection of contrast. Our films are thus timed in relation to the beginning of the contrast injection.

Example of application

A male, aged 60, with malignant carcinoidosis developed edema of the ankles. The question was whether this edema was due to a 'carcinoid' heart affection (of which there were no clinical indications) or whether the cause was mechanical, *e. g.*, as a result of carcinoid abdominal tumours. Venacavagraphy was performed under local anesthesia with the percutaneous introduction of polyethylene catheters into the right and left femoral veins. Fig. 2 a was exposed as the scale indicates 2.5 sec after the beginning of the contrast medium injection. Fig. 2 b shows contrast medium retention in the iliac veins as late as 9.5 sec after the injection.

Diagnosis: Displacement and reduction of the lumen of the vena cava with relative circulatory inhibition, probably due to right paravertebral tumour pressure.

(The investigation afforded valuable information for determining the therapeutic roentgen field.)

The apparatus provides a reliable and permanent timing of serial roentgenograms. It facilitates evaluation of the circulatory conditions, and the determination of contrast medium retention in vascular regions or tumours.

The manner in which the apparatus is connected to the photographic equipment involves no extra manoeuvres, and thus ensures reliable function.

SUMMARY

A description is given of a simple apparatus consisting of a 'clock' which provides automatic, direct time-marking of each individual exposure in serial roentgenograms.

ZUSAMMENFASSUNG

Eine Beschreibung eines einfachen Apparates wird gegeben. Dieser besteht aus einer 'Uhr', welche eine automatische direkte Zeitmarkierung jeder einzelnen Exponierung bei Serienröntgenogrammen gestattet.

RÉSUMÉ

L'auteur décrit un appareil simple consistant en une 'pendule' qui marque automatiquement et directement le temps où est pris chaque cliché dans les radiographies en série.

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR: PROF. K. LINDBLOM),
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ROENTGENOLOGIC DIAGNOSIS OF MEDULLARY SPONGE KIDNEY

by

Nils Lindvall

The term 'medullary sponge kidney' was coined in 1938 by LENARDUZZI to designate a condition in which the whole or parts of the medulla of the kidney presented a sponge-like appearance owing to the presence of multiple cysts and cavities formed by dilatation of collecting tubules. The occurrence of cysts in the medulla of the kidney has been mentioned occasionally in articles and textbooks of pathology for some 50 years (BEITZKE 1908, STAMMEN 1913, ASCHOFF 1936), but the clinical significance of the finding remained obscure until 1939 when LENARDUZZI published the first clinical and roentgenologic description of a case. Not until 1948 was the next case described (DAMMERMANN). The first detailed accounts of the condition and its morphologic picture were subsequently given by CACCHI & RICCI (1949) and GÜNTHER (1950). More recently a number of articles have been published on this subject, most of which are case reports and surveys of the literature. The largest series (12 cases) was the one presented by LHEZ in 1954.

The condition seems to be more common than would appear from the small number of cases which have been reported, and hence would seem to call for closer study, especially from the aspect of the roentgenologic findings, upon which the diagnosis must rest. This paper, therefore, deals with the roentgenologic appearances, as provided by an original case series, with particular reference to the problems of the differential diagnosis. The aetiology, the morphologic changes, and the clinical picture will be only briefly outlined here as they will be described in more detail in a future article. This brief outline is based on other authors' investigations.

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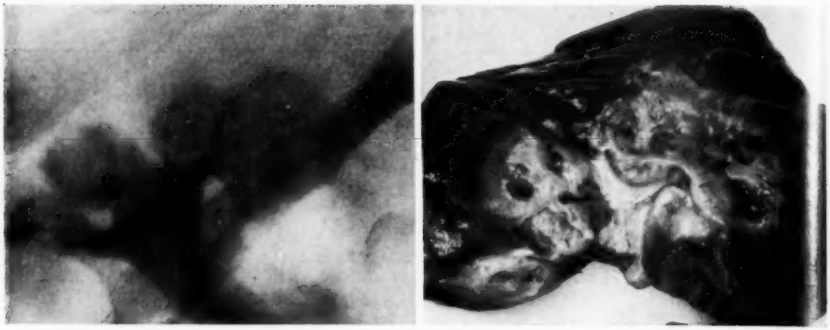

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Fig. 1. Right kidney. a) Urography. Typical sponge kidney, with contrast-filling of cavities in medulla, some of which contain small calculi. b) Specimen (resection). Upper part of medulla presents sponge-like appearance.

Aetiology. Medullary sponge kidney is generally regarded as a congenital malformation arising from a disturbance of the fusion of the nephrogenic tissue and the Wolffian ducts. Support for this theory is provided by the histologic appearances, the fact that in the absence of complications the changes show no progression for many years, and that concomitant malformations in the urinary tract together with cysts in the liver and pancreas are fairly often found. Other theories have been advanced: for instance, that the tubules are dilated by stasis produced by the precipitation of crystals of uric acid during foetal life (VERMOOTEN 1951).

Morphologic appearances. The changes are confined to the medullary substance and are not present in the cortex or the columns of Bertin; they may be found in one or more of the pyramids of one or both kidneys. All degrees of severity of the condition have been observed — from a few to an innumerable number of cavities distributed throughout the greater part of the medullary substance. In advanced cases the medulla has the appearance of a sponge (Fig. 1b), is paler than usual and contrasts with the normal cortex which has retained its colour. There is often an enlargement of the pyramids, in which the changes are situated, and of the associated calyces (Fig. 2, b and c). In cases of more general involvement the whole kidney is sometimes abnormally large. In cases displaying enlargement of the pyramids the cortex and columns of Bertin may be narrower than usual.

Microscopy discloses ectatic collecting tubules and cysts. The latter may be rounded or irregular in shape, in which case they are considered to be formed by the fusion of several small cysts. Areas of the epithelium of the tubules are embryonic in character. The cysts may be connected

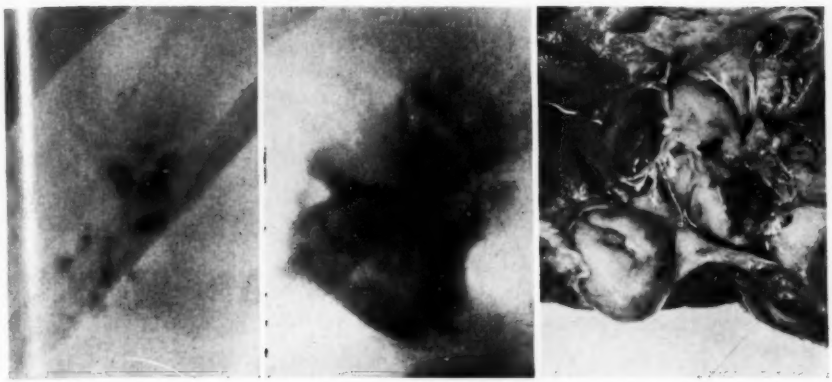

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Fig. 2. Right kidney. a) Group of calculi in upper part. b) Urography. The calculi are situated in filled cavities in the considerably enlarged papillae. c) Specimen (resection). The enlarged papillae bulge into the calyces.

with the tubules or the pelvis, or they may be isolated. The contents of the cavities vary, and masses of precipitated calcium salts and solid calculi have been found. The interstitial connective tissue is sometimes infiltrated with round cells. The cavities may be the source of infection and calculi. GÜNTHER considers that the stone formation is caused by infection. Inflammatory changes have also been encountered even in cases where there was no clinical evidence of infection. The cortex and mucous membrane of the renal pelvis present no appreciable changes apart from those of an inflammatory nature which may arise in connection with complications.

Clinical aspects. The changes themselves do not give rise to any clinical manifestations although such may be produced by infection and the formation of calculi, both of which are common. In uncomplicated cases the renal function is generally considered to be undisturbed, but in most of the reported cases there has been a slightly reduced concentration capacity.

The condition is more common in males than females and is generally observed in middle age. Only two cases in children have been described, one of them in a boy of 7 (GAYET 1953) and the other in a girl of 11 years of age (JOSSERAND et coll. 1952).

Material

An examination of the urographic records at Karolinska Sjukhuset for the periods 1940—42 and 1954—58 brought to light 31 cases in which there were characteristic appearances of medullary sponge kidney. Four further cases which had been examined

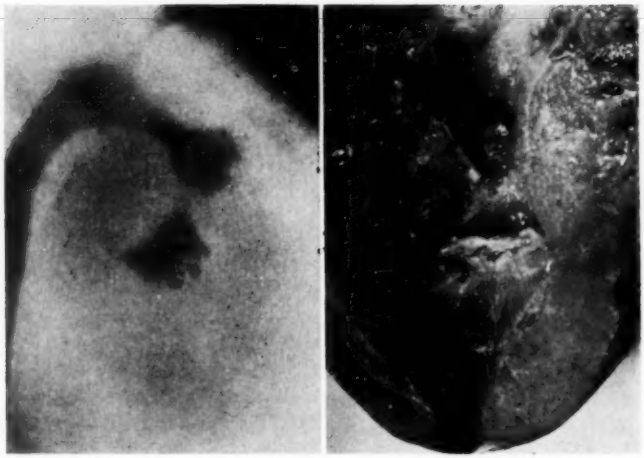

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Fig. 3. Left kidney. a) Urography. Small rounded cavities, some containing calculi, in lowermost papilla. b) Specimen (ectomy) showing small cavities in the papilla; a medullary cyst bulges into the lumen of other calyx.

at other hospitals were included. The complete series thus consisted of 35 cases, 21 of them males and 14 females. According to the roentgenograms the changes were bilateral in 23 cases and unilateral in 12; of these 6 were on the right side and 6 on the left. The diagnosis was generally made at about the time that the symptoms first appeared, the ages of the patients then ranging from 16 to 62 years, the large majority being between 20 and 35. The cases were occasionally followed for as long as 16 years, though there were several instances of single examinations. In all cases urographic examinations were performed, in some cases pyelography, and in two cases aortography was also included. Morphologic examination of resected or removed kidneys was performed in 9 cases and crystallographic and chemical analyses of the calculi in 14 cases. The renal function was examined by non-protein nitrogen determination, and in many cases also by concentration and clearance tests. Calcium balance tests were performed in 22 cases in which the patients were thought to have hyperparathyroidism.

Roentgenologic findings

In all cases the diagnoses were made from the urograms. The changes were of all grades, from cases of a few cavities in a single pyramid of one kidney to multiple cavities in all the pyramids bilaterally. Enlargement of the involved pyramids was observed in 31 kidneys (Fig. 2 b). In 13 there was an enlargement of the whole organ, the remaining kidneys were of normal size (MOËLL 1956). Even in parts of the kidney where no cavities were visible, there were in some cases enlarged papillae and general hypertrophy, suggestive of the presence of changes which had not been

directly shown (Fig. 7). The calyces of the enlarged papillae were also enlarged. The cortex and columns of Bertin were generally normal, but there were some instances of a thickening of the cortex (Fig. 9); in no case was there any definite reduction of the thickness of the cortex or the columns of Bertin.

The filled cavities varied in size and shape. In some cases there were stellated cavities, which were apparently dilated collecting tubules passing from the tip to the base of the papilla. These could be either very fine (Fig. 8 a) or coarse, in which latter event they penetrated further into the pyramid (Figs. 1a, 5 and 9b). In some cases the cavities were rounded and cyst-like, varying in size from those which were hardly visible to the naked eye to those the size of a pea (Figs. 3 a and 7 b); others were irregular or triangular (Fig. 4). In some instances it was observed that the surface of the papilla had a blistered appearance, though there were no filled cavities in the immediate vicinity (Fig. 5). As mentioned above, there may be cysts without communication to the surroundings and STAMMEN, and CACCHI & RICCI have found such cysts just beneath the mucous membrane of the papilla.

A typical feature of all the cavities was that they were the first structures to be filled, they appeared more distinctly on applying pressure to the ureter, the contrast medium remaining in the cysts when the pressure was removed and the pelvis emptied of the medium. This is what would be expected from the anatomy of the cavities.

In the few cases where pyelography was performed, only some of the cavities were filled with contrast medium (Fig. 6). It has been stated that none of the cavities can be filled by this procedure when no complication exists (LENARDUZZI, CACCHI & RICCI, BALESTRA & DELPINO). This difference between the findings in urography and pyelography may be ascribed to the normal functioning of the sphincters at the apertures of the tubules in uncomplicated cases so that reflux from the calyces is prevented (CACCHI et coll., BALESTRA et coll.). According to DI SIENO & GUARESCHI it should be possible at pyelography to fill cavities which are not outlined in urography. If the renal function is intact and the technique is properly performed, all the cavities which can be contrast-filled at pyelography should also be filled at urography.

In all but two cases, from one to several hundred calculi were present. Most of them were round and very dense; they were sometimes disposed in groups, and thus presented so distinctive a picture that the diagnosis was suggested even by the conventional film (Fig. 2 a). If at the same time there was enlargement of the kidney, the diagnosis could in some cases be made without recourse to urography (Fig. 7 a). In other cases the calculi were more diffusely distributed throughout the medullary substance and then the diagnosis could not be made without urography though it could be suspected if the kidney was enlarged (Fig. 9 a).

Fig. 4. Sponge kidney (right, of normal size) with irrregular cavities, some containing calculi.

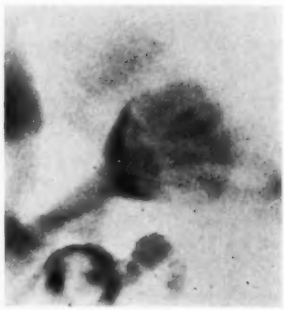

Fig. 5. Left kidney. Cavities similar to dilated collecting tubules, some containing elongated calculi. The surface of the papilla has a blistered appearance, indicating unfilled cysts.

In the two cases in which aortography was performed, normal vascular appearances and nephrographic effect were observed, as in the case described by ALKEN et coll. (1951).

During the observation period the only roentgenologic changes were signs of pyelonephritis, the formation, or disappearance of stones (after passing), or the appearance of hydronephrosis due to the passage of a calculus.

Malformations within the urinary tract, such as calyceal cysts and hypoplasia, were found in only 4 cases.

Differential diagnosis

The conditions and changes that might be roentgenologically confused with medullary sponge kidney are renal tuberculosis, papillary necrosis, calyceal diverticula and cysts, tubular stasis, and various forms of nephrocalcinosis.

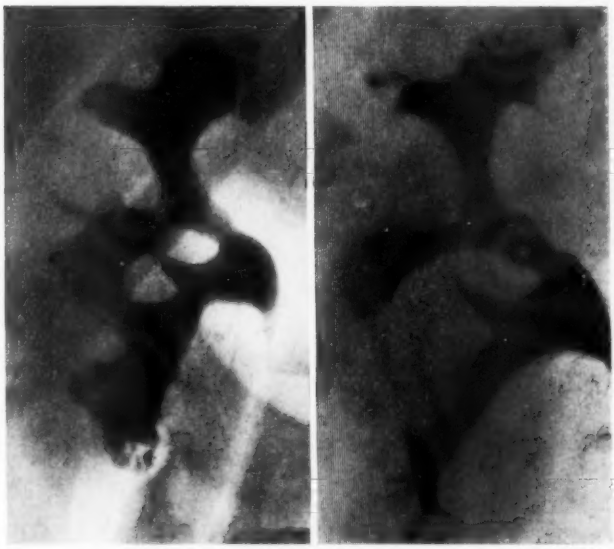

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Fig. 6. Right kidney. a) Urography. Pelvis normal in size. Sponge kidney with calculi in the cavities. b) Pyelography. Only some of the cavities are filled.

In *renal tuberculosis* there are often irregular deposits consisting of calcium salts precipitated in necrotic tissue. Calculi may be formed in the cavities but the cavities are rarely limited to the papillae. Owing to inflammatory impairment of the parenchyma just beneath the cavity, the latter is generally contrast-filled from the pelvis. There are also often changes in the calyces and the pelvis. In spite of the distinct pictures they present, medullary sponge kidney and renal tuberculosis are occasionally confused; this is true of earlier cases (DAMMERMANN) as well as in those of the present series. One case had previously been diagnosed and treated as renal tuberculosis in spite of a negative Mantoux reaction and the fact that no tuberculosis bacilli had ever been found (Fig. 6). During the 5 years that the patient was followed the roentgenographic appearances remained unaltered. By means of chemotherapy renal tuberculosis may be cleared up, with no residual changes other than a well defined cavity, which in urography may occasionally be filled with contrast medium from the parenchyma. Such a case, in which the cavity is entirely within the pyramid, may therefore resemble an atypical case of medullary sponge kidney with only one cavity visible, though this did not occur in the present series.

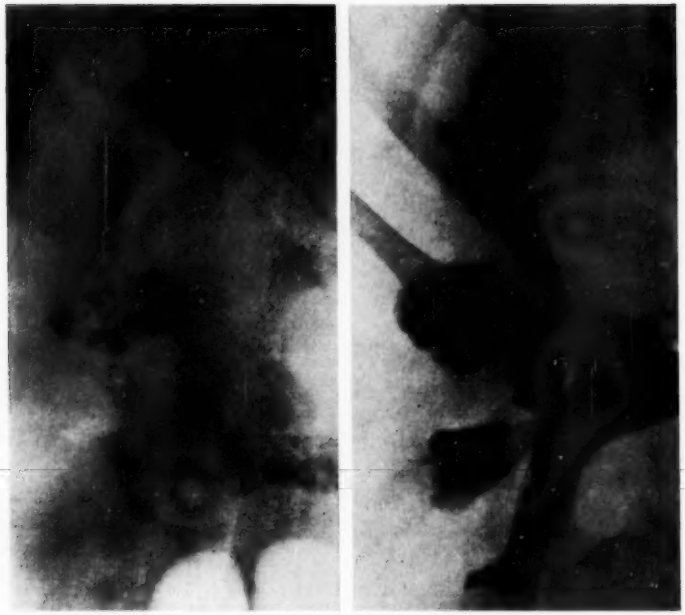

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Fig. 7. Right kidney. a) The kidney is considerably enlarged. Calculi distribution typical of medullary sponge kidney. b) Urography. The calculi are situated in medullary cavities. No calculi or cavities in the lower papillae are visible. Biopsy, however, showed typical changes even there.

In the medullary form of *papillary necrosis*, cavities are formed in the tips of the papillae, and these are visible early in urography; the fornix of the calyx may be intact, at least at the beginning. Calculi are sometimes formed in these cavities (LAGERGREN & LINDVALL 1958). Such a case would resemble one of medullary sponge kidney with a single cavity in each papilla. An extreme case of this nature has never been reported.

Calyceal diverticula and cysts are the first to be filled in urography and may contain calculi. Nevertheless, they lie between the pyramids and are connected with the calyces in the region of the fornix. They are regarded as a kind of malformation, and it is not known whether there is any connection between these and true sponge kidneys.

So-called *tubular stasis* of all forms may according to VERMOOTEN be regarded as cases of abnormally wide collecting tubules of the same type as in sponge kidney; the condition must in fact be regarded as a normal

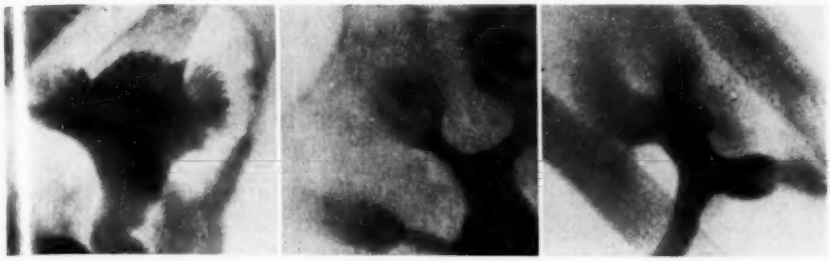

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Fig. 8. a) Sponge kidney. Urography. Striated cavities in the papillae (= dilated collecting tubules). b) Normal kidney. Urography. Tubular stasis with a striated appearance. At following urography no tubular stasis. c) Normal kidney. Urography. Tubular stasis of ordinary type.

finding. Its causes are not entirely known. The roentgenogram generally shows a structureless cloud of contrast medium in the papilla (Fig. 8 c), but there may sometimes be radiating striations (Fig. 8 b). The phenomenon generally occurs soon after the application of pressure to the ureter and disappears when this is released. A similar appearance can sometimes be observed soon after the contrast medium has been injected and just as it begins to accumulate in the calyces; it soon disappears but returns on applying pressure. Whether or not the striation that is sometimes seen in tubular stasis is due to some of the tubules being wider than normal is not known. As GÜNTHER has pointed out, the occurrence of a few ectatic tubules in one or two papillae is not an uncommon finding; this has been verified in the present study by examination of a large number of specimens. Widened tubules cannot, however, be distinguished in the same way as in medullary sponge kidney (Fig. 8 a), nor do the tubules remain filled after removal of the pressure. Occasionally, however, the tubular stasis with the striated structure remains after pressure is removed but in our series this was observed only in cases in which there was spasm within the renal pelvis and calyces; on subsequent examination when no spasm was present, the phenomenon did not recur.

In cases with multiple calculus deposits, other forms of so-called *nephrocalcinosis* must be considered. The term nephrocalcinosis covers several unrelated morbid conditions, beyond the fact that they give rise to calcification in the kidneys. The most common of these conditions is hyperparathyroidism, in which various types of calcification occur, such as true renal calculi, parenchymal calcification, and a combination of both. These parenchymal calcifications are situated in the epithelium of the tubules, in the tubules, or in the interstitial tissue (HELLSTRÖM 1955). There may sometimes be slight dilatation of the collecting tubules when these are the sites of calcification, but the latter are then primarily

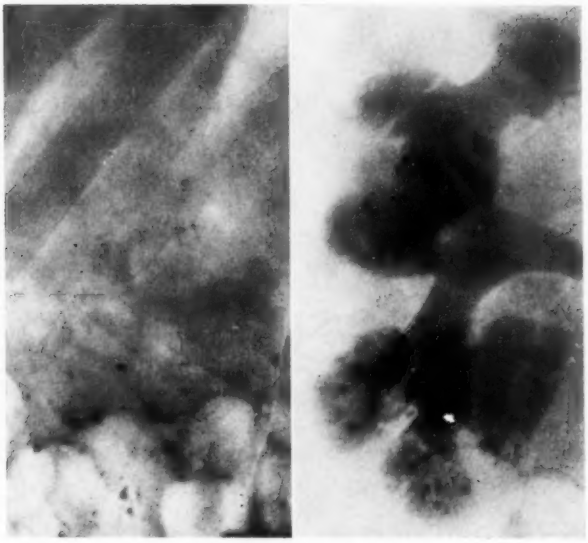

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Fig. 9. Right kidney. Considerable enlargement of the kidney and pelvis. a) Small calculi diffusely distributed throughout the medullary substance. b) Urography. Cavities in all the pyramids, some with the appearance of dilated collecting tubules, and some more like cysts. The calculi are situated in the cavities. Enlarged papillae.

formed concretions and not such produced in pre-existing cavities, as in sponge kidney; they are also more irregular (Fig. 10). If the deposits have been passed in the urine, no residual widening of the tubules is evident. In hyperparathyroidism accompanied by nephrocalcinosis there is also in most cases a reduction of the renal function, manifested as reduced density of the filling in the urogram, and finally there may be a contraction of the kidney.

In renal tubular acidosis (Reynolds 1955) another type of nephrocalcinosis occurs. This type of nephrocalcinosis may be found in children and even in adults. In some, the calcifications are very typical with multiple small concretions, generally rod-shaped, which are not located in cavities (Fig. 11). These cases will be discussed in greater detail in a future article.

Discussion

The increasing number of case reports in recent years suggests that medullary sponge kidney is more common than has previously been

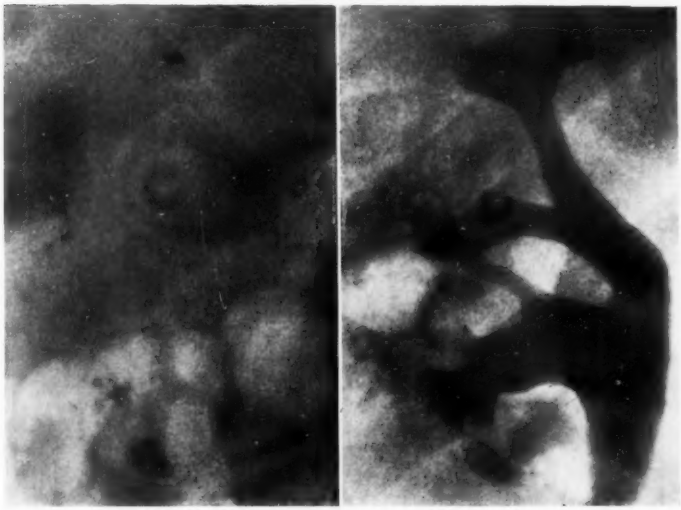

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Fig. 10. Hyperparathyroidism. Right kidney. a) No enlargement of kidney. Multiple irregular calculi. b) Urography. Density of pelvis normal. The calculi are situated in the papillae, but there are no filled cavities.

supposed. This fact may be ascribed to insufficient acquaintance with the roentgenologic appearances of the changes.

The clinical picture is determined solely by the complications, and the diagnosis will therefore rest with the roentgenologist. The diagnosis is facilitated by the fact that the changes do not appreciably affect the excretion of contrast medium. In spite of wide variations, the changes are so characteristic in their location and appearance in urography and pyelography that the findings may be regarded as pathognomonic. The changes observed in the present series show greater variations than those earlier reported. In no case was thinning of the cortex and the columns of Bertin observed, although this has been described as rather a common feature. Formation of calculi in the cavities was absent in two cases only. This frequent occurrence of calculi distinguished the series from the cases published earlier. In LHEZ's series, for instance, calculi were found in only 2 out of 12 cases. The reason for this difference is obscure. In the great majority of cases the appearances were unchanged during the period of observation, apart from an occasional instance of the appearance of new calculi or the disappearance of calculi after they had been passed. In some cases, with an observation period of several years, hydronephrosis and pyelonephritis developed following

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Fig. 11. Renal tubular acidosis. Left kidney. a) Small rodshaped concretions in groups in the medulla. b) No enlargement of kidney or pelvis. Density of pelvis normal. The concretions are situated in the papillae. No cavities.

the repeated passage of calculi. This development is illustrated by the case shown in Fig. 9.

This case represented a patient in whom one kidney had been removed a year after the onset of symptoms due to complications arising from the presence of calculi. Marked hydronephrosis subsequently developed in the other kidney owing to the repeated passage of calculi; moreover, there was pyelonephritis. There was also serious anuria caused by the presence of calculi in the ureter. Resection of the inferior pole of the kidney was performed and the calculi in the other papillae were removed. A follow-up one year later showed no recurrence of symptoms.

The passage of calculi was a very common complication, which sometimes resulted in temporary incapacity, and in the case described above even threatened the life of the patient. This risk of complications due to calculi means that an early diagnosis must be made, since resection may be justified, especially in cases of partial involvement. Removal of the affected area should result in complete cure. In the cases illustrated in Figs. 1 and 2 resection of the superior pole of the kidney was undertaken and both were symptom-free afterwards. The patient in Fig. 2 had had symptoms solely due to renal calculi, with no clinical evidence

of infection. At biopsy a typical sponge kidney with acute inflammatory changes and calculi was found. Eight years after the operation the patient was still symptom-free.

With the purpose of studying the occurrence of symptomless cases a scrutiny was also made of films from all urographies and pyelographies performed during the periods 1940—1942 and 1954—1958. No such cases could be found. Only in one case could the changes be regarded as incidental findings, while in all the other cases the examination was prompted by symptoms associated with the involved kidney. This isolated case was of a patient with tuberculous changes in the superior pole of the left kidney; changes typical of sponge kidney with calculi in the inferior pole were present (Fig. 3). The patient was followed for 6 years before nephrectomy was performed; during this period the sponge kidney changes were unaltered while the tuberculous changes somewhat progressed. Biopsy showed typical sponge kidney appearances in the lower pole of the kidney, but no evidence of tuberculous inflammation. One cannot be sure in this case, however, that the inflammation may not have had its origin in similar changes in the upper pole.

Conclusions

Medullary sponge kidney is so common that it deserves more attention than it has hitherto received. Owing to complications the condition will generally give rise to symptoms, the most common of which is the passage of stones. The roentgenologic appearances are characteristic and permits the establishment of the diagnosis. A correct diagnosis of medullary sponge kidney may be of value in the choice of therapy, as resection may result in a complete cure.

SUMMARY

A survey is made of a series of 35 cases of medullary sponge kidney. The characteristic roentgenologic appearances are described and the problems presented by the differential diagnosis discussed.

ZUSAMMENFASSUNG

Der Verfasser gibt einen Überblick über 35 Fälle mit Markcystennieren. Das charakteristische röntgenologische Aussehen wird beschrieben und die Probleme, welche sich differentialdiagnostisch bieten, werden besprochen.

RÉSUMÉ

L'auteur présente une série de 35 cas de "rein en éponge". Il en décrit les aspects radiologiques caractéristiques et examine les problèmes posés par le diagnostic différentiel.

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RADIATION CATARACT FOLLOWING FRACTIONATED RADIUM THERAPY IN CHILDHOOD

by

C. F. Qvist and *B. Zachau-Christiansen*

Recent nuclear physics developments have greatly increased the interest in the hazards of ionizing radiation in medical radiology. Attention has been directed particularly to the radiosensitive cells of the gonads, the haemopoietic tissues, and the lens of the eye.

CHALUPECKY in 1897 described the first experimentally induced cases of radiation cataract. Eight years later, GUTMAN & TREUTLER reported the first case of radiation cataract in man. In 1931 BLEGVAD reported the first case which had occurred in Denmark. In the same year DESJARDIN and in 1942 POPPE published comprehensive surveys on this subject. Thus, in the early forties less than 100 human cases had been reported, and in most of them data regarding the radiation dose were scanty or lacking. During the past decade about a further 150 cases have been published (1, 5, 6, 12, 15, 18, 19). In addition, there are more than 400 cases as sequelae from the Japanese atomic bomb explosions (7, 13).

While the early cases were invariably induced by roentgen rays or radium, many recent cases have been caused by neutron irradiation. This form of therapy has been used to some extent in the United States, and

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physicists working on cyclotrons have received neutron irradiation. The atomic bomb victims received gamma as well as neutron irradiation (20).

About 1950 it was assumed that a lens dose of 500 r was the minimum cataract-inducing dose in human subjects. Later, lower doses, 300 r daily for two days (COGAN & DREISLER 1953), and a single dose of 200 r gamma rays (MERRIAM & FOCHT 1957), have been found to be capable of producing the same effect. The latter authors have reported 100 cases following roentgen or radium therapy. In their opinion, fractionation of the dose is of great importance; if the treatment extended over a period of from 3 weeks to 3 months (number of sittings not mentioned) the threshold value was found to be 400 to 450 r (gamma radiation or roentgen radiation in the 200 to 250 kV range); if the fractionation was extended beyond three months, the minimum total dose was 550 r. They also found that 1,150 r was capable of inducing cataract in all cases and that infants under one year of age were more susceptible than adults, showing a higher frequency of manifestations at the same dose level than older subjects, a shorter latent period, and a larger number of progressive cataracts.

The latent period has generally been reported to be 2 to 5 years, but periods of up to 13 years have occurred.

In neutron irradiation, the cataractogenic dose is lower; HAM reported 45 rep. From statements regarding distance in KANDORI & MASUDA's patients it is evident that according to the radiation doses reported by NEEL & SCHULL at different distances from the hypocentres of the atomic explosions, the threshold value has been as low as 10 rep, provided that the distance measurements are correct.

With beta radiation MERRIAM (1955) found cataract after doses of 230 to 1,120 rep.

As far as experimental work is concerned, threshold values of 15 r have recently been found in mice (UPTON et coll. 1953), and at 45 r all developed cataract. It has been reported (27) that 1 to 2 MeV neutrons are twice to thrice as effective as 250 kV roentgen irradiation and three to four times as effective as 1.2 MeV gamma rays in inducing cataract with the same quantity of energy.

Pathologic changes. The first histologic studies of lenses affected with radiation cataract were carried out less than 30 years ago. GREDZIELSKI thought the lesions represented lens proliferation, but the following year LEINFELDER & KERN reported that they were degenerative lesions associated with swelling of the lens fibres; this has been confirmed by subsequent investigations (5, 23, 24, 25). The irradiation is followed by the development of pyknotic and fragmented nuclei in the epithelial

cells of the lens after some days' inhibition of the mitotic activity. Later, the swollen lens fibres contain small vacuoles. Such degenerated cells do not disappear from the avascular lens, and they form the opacities apparent on ophthalmologic examination. The first gross evidence is a small dot at the posterior pole of the lens, a dot which may increase in size; further dots and vacuoles may arise, arranged so as to form a more translucent central area. In severe cases there are also granular opacities and vacuoles in the anterior subcapsular part of the lens.

The fact that the degenerative changes arise at the equator has been most clearly demonstrated by McDONALD et coll. Using small neutron beams they found that this region was 10 times as sensitive as the epithelial cells adjacent to the anterior pole.

As a rule, the opacity is only visible in the slit lamp, and does not generally give rise to essential visual impairment. In a Japanese series (13) 55 % of the cases had normal vision and only 3 % to 4 % essentially impaired visual acuity.

Present investigation

The great majority of human cases reported occurred after medical irradiation and affected elderly patients with malignant diseases. We therefore felt that it would be of interest to conduct a follow-up study on subjects who had received radium therapy to the face, mainly during infancy, for benign diseases with doses which, at our present stage of knowledge, might be assumed to have induced cataract. To this end, we perused the case records of the Radium Centre for patients treated with radium for haemangiomas during the period 1913 (when the Radium Centre was established) to 1933. This period was chosen for several reasons: In the first place, this treatment has been carried out (successfully) with much lower doses during the past 25 years. Owing to the long follow-up period we could be sure that the cataracts which we did find were stationary. In addition, we had a possibility of detecting possible radiation-induced skin cancers.

During the period concerned a total of 1,417 patients had been treated for haemangioma and in 855 of these the lesion had been situated in the region of the head; in these cases, the dose in the nearest lens was calculated in r units.

In cases where the radium preparations had been placed approximately parallel to the equator of the eye, we calculated the dose from the stated area of the preparation by means of PATERSON's tables for converting mg/curie hours to r. In cases of small preparations more than 2 cm from the eye, we consider the preparation as a point, calculating the lens dose on the assumption that 1 mg RaCl at a distance of 1 cm

Tables 1—5

Case No.	Age at 1st treatment (yrs)	Dose to lens in r*	Treatments: Number	Treatments: Duration months	Single dose or range of single dose to nearest eye	Follow-up period (yrs)	Ametropia	Vision	Other finding
Table 1. *Cataract after treatment for haemangiomas with radium*									
1	5/12	*s* 3,230 *d* 200**	5	22	1,080—320	34	*d* ÷ 2.5	—	*s* post. cortical cataract
2	10/12	*d* 3,210 750**	15	21	210— 50	42	*s* ∴ 10.0	*d* finger-counting	*d* cataract covering lens
3	4/12	*s* 1,610 *d* 400**	4	10	1,200— 60	38	—	—	*s* post. polar cataract *d* + *s*: astigmatism
4	2,12	*s* 1,380 *d* 90	2	2	690	32	—	*s* 6/36 *d* 6/9	*s* small opacities in both capsules
Table 2. *Other types of cataract*									
5	31	*s* 640 *d* 290**	1	0	—	40	*d* + *s* + 2.0		*d* + *s* senile cataract
6	8	*s* 280**	17	48	35— 10	32	*d* + *s* ÷ 1.25	—	*s* small opacity not like rad. cataract
7	3/12	*d* + *s* 150**	6	7	25	40	—	—	*s* cong. cataract
Table 3. *Other diseases of the eyes*									
8	1/12	*s* 380 *d* 25**	3	6	170— 40	37	*d* + *s* ÷ 2.5	—	—
9	15/12	*s* 390 *d* 300**	3	9	130	40	*s* ÷ 1.5 *d* ÷ 2.5	— —	—
10	4/12	*s* 990 *d* 60	4	9	330—110	24	—	*s* 1/60 *d* 6/6	
11	3/12	*s* 840 *d* 210	4	15	420— 80	35	—	*s* 6/18 *d* 6/9	—
12	25	*s* 780 *d* 30	4	8	250—170	33	—	*s* 6/36 *d* 6/6	strabism
13	2	*d* 540 *s* 140	11	34	70— 5	26	*s* ÷ 20.0 *d* + 1.0	*s* 6/60 *d* 6/9	strabism
14	2/12	*d* + *s* 270	3	13	240— 15	29	*d* + 4.5 *s* + 3.0	—	—
15	3/12	*s* 270 *d* 140	6	18	90— 5	24	—	*s* 6/24 *d* 6/6	—
16	4/12	*d* 250 *s* 30	3	8	125— 60	26	*d* + *s* ÷ 2.5	—	—
17	3	*s* 200 *d* 10	4	9	110— 15	25	*d* + *s* ÷ 1.0	—	—
18	16/12	*d* 120 *s* 60	3	13	40	25	*d* ÷ 11.0 *s* ∴ 10.0	—	—
19	5/12	*d* 100 *s* 15	4	10	25	25	*d* + 9.0 *s* + 10.0	—	—
20	5/12	*s* 100 *d* 25	3	11	40— 30	32	*s* + 4.0 *d* + 8.0	—	—

Tables 1—5 (Continued)

Case No.	Age at 1st treatment (yrs)	Dose to lens in r*	Treatments		Single dose or range of single dose to nearest eye	Follow-up period (yrs)	Ametropia	Vision	Other findings
			Number	Duration months					
Table 4. *Skin cancer in the scar*									
2	10/12	180	4	11	90— 10	31	—	—	skin dose: 1,180 r
Table 5. *Other patients*									
22–26	2/12—4/12	750—110**	13—4	23—7	270— 10	42—35	—	—	—
27–28	9—14	1,140—340**	11—4	24—18	280— 5	40	—	—	—
29–48	1/12—1 average 4/12	660—110	10—3	72—7	200— 3	31—21	—	—	—
49–57	1 1/2—9 average 3 1/2	320—100	9—2	34—4	310— 3	34—27	—	—	—

d — right eye; *s* — left eye; * only one value means that to the nearest eye; ** dose not definitely known because of incomplete data, minimum dose given.

with a filtration of 0.5 mm Pt gives 8.4 r (21), and then using the law that the dose is inversely proportional to the square of the distance. In cases of doubt, both calculations were used, but in practically all cases they gave very similar results. However, the former method was preferred. Large preparations were divided into 3 to 5 smaller fields, and the lens dose for each field was calculated as described above. Correction was made for the Pb filtration according to the usual rules.

It must be mentioned that MERRIAM & FOCHT (1957), determining the lens dose during roentgen and radium irradiation, have performed phantom measurements; in the cases treated with radium they found agreement between the measured doses and the doses calculated according to the law of distance.

Since the distance between the nearest lens and the treated area is not evident from our case records, we measured the distance from the eye to a number of sites on the head of normal children aged 3 months, 6 months, one year, 4 years, and 7 years, and of adults. By comparing these findings with the situation of the lesion according to the description, drawing, or photo in the case records, we determined the distance. Owing to inaccurate statements of dosage during the first 9 years of the period, we divided the analysis into two parts, only a presumed dosage, calculated as a minimum dose, being stated in the earliest cases.

Results and Discussion

Out of the 855 patients 112 were found to have received a lens dose of more than 100 r in the eye that received the larger dose: only these patients were after-examined. From the national registries we traced the present addresses of 96 patients, while 16 had died during the follow-up period or could not be identified from the rather incomplete data supplied by the oldest case records.

The patients were asked to appear for a follow-up examination. Out of 55 who lived in Copenhagen and its neighbourhood 47 arrived, whereas only 9 out of 41 living in other parts of Denmark seemed interested. Furthermore, one patient was examined by an ophthalmologist at his place of abode (a home for the mentally deficient). Thus, the total number of patients included in the follow-up was 57. Among them, only 4 cases of unmistakable radiation cataract were found. (See also Tables 1 to 5.)

Our rather small series did not contribute essentially towards answering the question regarding the threshold value for the induction of radiation cataract. However, MERRIAM & FOCHT's finding that a total dose to the lens of 1,150 r is necessary for including radiation cataract in all radiated patients applies to our patients too, the minimum cataractogenic lens dose being 1,380 r (Case 4), the maximum non-cataractogenic dose to infants 990 r (Case 10), and to children of school age 1,140 r (Case 27). Accepting the view that it is a single, particularly large dose which is cataractogenic since a cumulative effect, as seen in mutation induction on radiation of the gonads, has not been demonstrated in the previously mentioned experimental investigations, it will be observed that the minimum safe single dose in our series is 690 r. The dose of 210 r to Case 2 is not a definite minimum value (cf. what has been stated above regarding inaccuracies in our oldest case records). In those of our patients who did not develop cataract, the maximum single dose to infants was 420 r (Case 11).

Attention must be drawn to Cases 6 and 7 in Table 2. Especially in the former, the opacity might have been interpreted as a radiation cataract and, if so, might have completely upset the conclusions. Since, for the reason just mentioned, the lens dose given is merely a minimum value, and the opacity did not resemble the changes generally seen in radiation cataract, we dare not attribute any significance to this isolated finding considering that a cataract may be due to so many different ætiologic factors.

Like other authors, we found that as a rule radiation cataract does not essentially impair vision, as only one patient had real visual im-

pa ment, another some impairment in the affected eye, and the remaining tw normal vision.

Whether the infant lens is more sensitive than the adult lens to ind ction of radiation cataract cannot be decided from our studies. It do not appear likely, but it must be remembered that our period of tre tment is very long and the single doses rather small.

Another two factors are striking, however. We had three patients (Ca es 10, 11, 15) with impaired visual acuity, most marked in the eye wh h had received the larger dose. This phenomenon was not explicable by cataract, strabismus, or other aetiologic factors. It is reasonable to ass me, therefore, that radiation of an infant's eyes by large doses of ion zing rays (in these cases 990 to 270 r) may have a detrimental effect on the retinal perception, although of course the numbers involved are too small to allow of any conclusions.

It is strange, moreover, to find so many cases of relatively marked refraction anomaly, myopia as well as hypermetropia. According to the Scandinavian textbook of ophthalmiatrics (28) only about 2 per cent of the patients would be expected to exhibit these anomalies. In the present series 11 patients (Cases 1, 2, 5, 8, 9, 13, 14, 16, 18 to 20), or 19 per cent, had ametropia exceeding $\pm$ 2.

Even though it might be imagined that the anomaly was not present in any of the 39 patients not included in the follow-up the incidence would be 11 % or still distinctly higher than in a normal series, as the lower 99 % 'confidence' limit of the named frequencies is 8 and 5 per cent. It must be remembered, however, that up to 50 per cent of grammar school pupils have been found to be myopic. Since, however, both forms of ametropia were of approximately the same frequency, and since the series does not include strictly academic individuals — although there were a few children of teachers — this factor cannot be operative here. It must be permissible to assume, therefore, that the radiation may have been the cause of the visual changes by acting upon the growth of the eye in an unknown way. We are unable to advance any proof, however, particularly as no constant relationship was found between the degree of ametropia and the radiation dose. In one patient indeed the most marked ametropia was found in the eye which had received the smaller radiation dose.

Any consideration of the skin condition, haemangioma, for which the radiation was given is outside the scope of the present paper. The interested reader is referred to the recent, brief and excellent review of MacCallum & Martin. It was impossible to classify the treated haemangiomas from the data in the case records, but the series included capillary as well as cavernous varieties.

We agree with MacCallum & Martin that radium therapy in the

form given at that time was not particularly satisfactory. Nearly all the patients examined had atrophy of the skin and subcutaneous tissue although only a few expressed dissatisfaction with the treatment. In this connection it may be mentioned that a total of 24 out of the 57 patients had received skin doses higher than or equal to that received by the patient in Case 21. In other words, the radium therapy was administered in doses essentially higher than the ionizing radiation which is used today for treating this condition. Only Case 21 exhibited signs of skin cancer at the follow-up. Although our control period is long, it is of course possible that other cases of skin cancer my arise. Development of cancer has been reported as late as 49 years after a skin dose of roentgen rays of 1,000 r (20).

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SUMMARY

The authors discuss radiation cataract in a series of 57 cases, mostly infants, treated with radium for cutaneous haemangiomas of the head during the period 1913—1933. Four were found to have developed the condition; the series included many cases of visual impairment.

ZUSAMMENFASSUNG

Die Verfasser diskutieren das Vorkommen des Strahlenkataraktes in einem Material von 57 Patienten, meist Säuglinge, welche während der Jahre 1913—1933 wegen kutaner Hämangiome des Kopfes mit Radium behandelt worden waren. Vier von diesen Patienten entwickelten einen Strahlenkatarakt; in vielen Fällen trat eine Herabsetzung des Sehvermögens auf.

RÉSUMÉ

Les auteurs étudient la cataracte due aux radiations sur une série de 57 cas, en majorité des nourrissons, traités par le radium pour des hémangiomes cutanés de la tête au cours de la période 1913—1933. Ils ont trouvé quatre qui présentaient cette affection; la série comprenait de nombreux cas de déficience visuelle.

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VARIABILITY OF RADIATION DOSE-EFFECT REGRESSIONS

by

Heinz Oeser and *Ernst Krokowski*

The dependency of biologic effects upon the conditions of irradiation has been studied experimentally in the rabbit eye. Cataract and weight changes of the optic lens are examples of somatic radiation damage. Earlier investigations have shown the possibility of inducing a cataract of the optic lens by roentgen radiation. Reports on the doses which are capable of producing cataracts, however, differ widely. MERRIAM and FOCHT have recently reported radiation damage to the human eye with doses as low as and even less than 200 r; a radiation cataract was produced in several cases.

In our own experiments we have used rabbits from the strains of the Max-Planck-Institut für vergleichende Erbbiologie und Erbpathologie (Prof. H. NACHTSHEIM), Berlin-Dahlem. The work was performed in collaboration with U. EHLING.

Dose measurements were carried out with a scintillation dosemeter with sodium salicylate as the scintillation substance. The volume of measurement was 1.137 ml, the diameter 6.4 mm, and the sensitivity $6 \cdot 10^{-3} \frac{\text{r/min}}{\text{Skt}}$. By comparative measurements a wave-length independency for the range from 35 to 200 kV could be confirmed.

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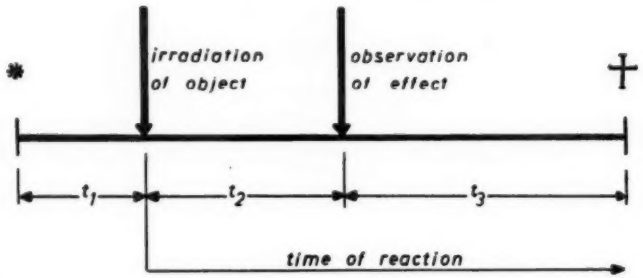


Diagram 1. t_1 — age at date of irradiation; t_2 — interval between irradiation and observation of effect; t_3 — interval between observation date and end of life; $t_{total} — t_1 + t_2 + t_3$.

The development of radiation cataract as regards degree, extent, and course depends exclusively upon the dose absorbed by the target organ. The quality of the radiation has no influence. The loss of transparency occurs the earlier, the more intensive, and the larger the absorption of the dose. As a threshold value for the loss of transparency of the lens, about 200 rad was found to be in good agreement with observations on the human eye. A recover from such damage, once it has been induced, was never observed in our experiments.

The age of the irradiated animals proved to be of great importance in the extent of the damage induced. In young animals damaging doses have been observed at considerably lower levels than those so far reported in the literature. Inhibition of growth and disturbances of water metabolism and water balance of the lens have been observed as additional effects of irradiation. The influences of dose, age (t_1), and observation date (t_2) on these manifestations were analysed, and the conclusions drawn concerning the question of dose-effect regression are now presented.

Radiation dose-effect regressions

Every experiment appears in the main to consist of two aims, namely (1) of influencing the experimental subject and (2) of observing the effects. It is characteristic of biologic experiments that these effects belong to different periods of an individual life.

As can be seen from Diagram 1 the dates for the experimental interference and for the registration of the effect stand in relation to the total course of life of the biologic subject. The quality and extent of the reaction to the irradiation will be dependant upon t_1 and will develop within the interval t_2 and t_3. It is, however, not merely the absolute length of t_1 and t_2 that determines the individual reaction, but also the total time

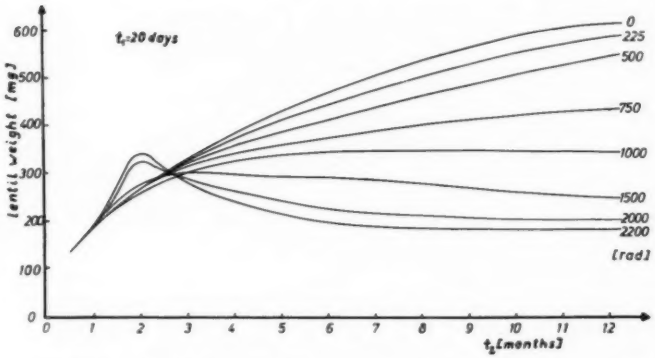


Diagram 2. Weight changes of the optic lens caused by different radiation doses in relation to the interval between irradiation and observation of effect.

of life (t_{total}) of the subject, which implicates a variety of functional and developmental phases. Especially t_{total} has to be taken into consideration if irradiation effects in biologic subjects are to be compared. The time relation $t_1/t_2/t_{total}$ will thus exert a decisive influence on the form that the dose-effect regression will take. The vitality *i. e.* the dynamics of the vital processes, which will here be termed the 'degree of vitality' is characterized by this time relation.

Our experiments with the rabbit optic lens seemed suitable for the investigation of the influence of t_1 and t_2 on certain irradiation effects. For this purpose the results of the experiments have been divided into two groups. In the first group, t_1 has been chosen as a constant. The weight of the lens has then been determined at different intervals after irradiation.

Diagram 2 shows the mean weight of the lenses as depending on the observation date t_2. The parameter is given as the dose absorbed. Each of the different doses results in a certain regression curve of the weight of the lens on the date of observation. The weight is determined by the extent of the inhibition of growth, loss of substance and disturbance of the water balance.

Both the Diagrams 2 and 3 have been constructed on the mean values of results published in earlier reports.

During the first month following irradiation, the lens growth seems to remain unaffected. Within the second month, however, a definite influence on the weight can be observed. Doses from 500 to 1.000 rad cause a reduction, while larger doses result in an increase of the mean weight of the lenses. At about 80 days after irradiation all regression lines seem to intersect, as can be seen from Diagram 2. This means that

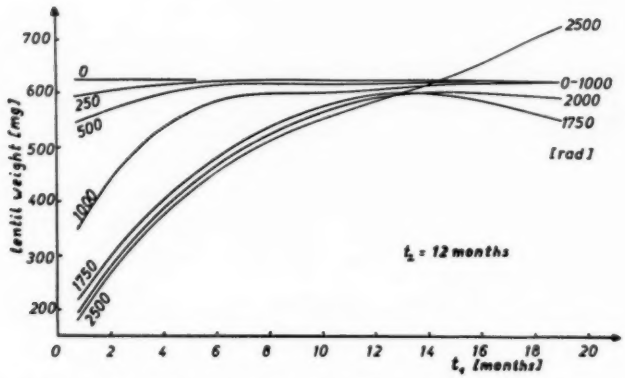


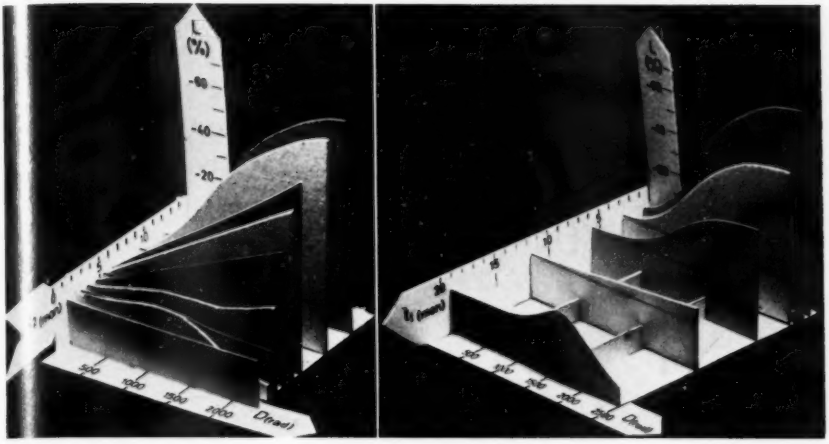
Diagram 3. Weight changes of the optic lens caused by different radiation doses in relation to the age of the animals.

at this observation date — independent of the irradiation dose — a normal lens weight will be found. This seeming independence on the dosage is brought about by the fact that with low doses a reduction of the lens weight cannot be observed at this time, while with high doses the initial fluid increase of the lens is balanced by a loss of substance. At later observation dates each irradiation dose causes a more or less severe decrease in the mean weight of the lens.

In the second grouping of the experimental date, t_2 is kept constant while t_1 serves as the variant. The lens weight of the rabbits irradiated at different ages has been determined one year after irradiation (Diagram 3). The reduction in weight of the lens has been found to be the smaller the more advanced the age of the animal at the time of the radiation. For $t_1 = 13$ months, a point of intersection for all regression lines is recognizable. Irradiation of still older animals with doses up to 200 rad results in an increase in the lens weight.

The importance of these experiments becomes evident when the dosage effect regressions are derived from Diagrams 2 and 3.

The dependence of the dose-effect relation on t_1 and t_2 can only be recognized by a three-dimensional graph. In Fig. 1 a is demonstrated the percentage change in the lens weight (L) depending upon dosage absorbed (D) and observation date (t_2). An initial dose independency appears which corresponds to the intersection point of the curves as shown in Diagram 2. With an increasing t_2 a sigmoidal dose effect regression becomes apparent. At observation dates from 4 to 6 months after irradiation, a linear dose regression is found. At later observation dates this linear dose-effect relation again changes into a sigmoid relationship.



a b

Fig. 1. Dose-effect regressions resulting (a) from the data of diagram 2, and (b) from the data of diagram 3.

Fig. 1 b shows a three-dimentional graph of the percentage change in the lens weight (L) in relation to dosage (D) and age at irradiation (t_1). By comparison with Fig. 1 a it will be seen that in both cases the typical succession of the curves is repeated, provided the direction of the co-ordinate of t_1 is taken opposite to that of t_2. This means that for every single age group of the experimental animals an almost identical reaction pattern of subsequent dose effect relation exists. An indifferent phase is followed via intermediate stages, at first by a definitely linear regression phase and finally by a sigmoidal relationship. Within this general reaction pattern the speed of succession of the single phases is determined by the irradiation age of the animals. The type of reaction at each observation date is the more advanced, in terms of the general time reaction pattern, the younger the animals at the time of irradiation.

As far as the question of the existence of a threshold value is concerned, the observation of a linear dose-effect relation with a somatic radiation damage — namely weight changes in the optic lens — seems to be especially important. A statistical analysis was therefore performed by the biometrician of our institute (PAUL KÜHNE) on one of the characteristic examples. This consisted of 32 values of measurements and 8 controls. The conditions of linearity for the regression function are evident from Diagram 4.

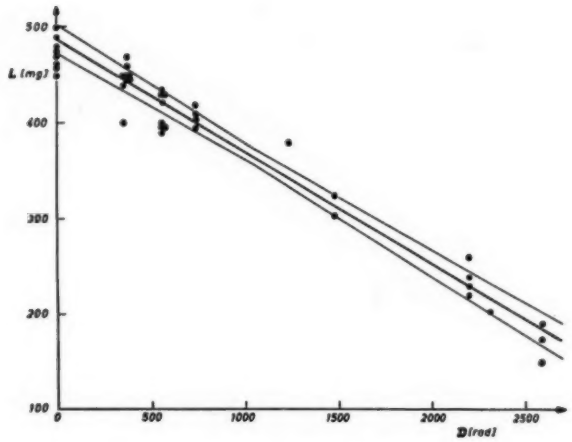


Diagram 4. Linear regression phase of lens weight on the dose of irradiation (t_1 — 20 days; t_2 — 5 months).

The difference in mean lens weight between the 8 controls (472.875 $\pm$ 16.9 mg) and the test group of 9 animals irradiated with 362 rad — mean doses of 352 and 370 rad — (445.555 $\pm$ 19.2 mg), with $t = 2.63$ and 15 degrees of freedom, has been found significant at a level of $P < 0.02 > 0.01$. Thus it seems certain that any innoxious threshold dose, if indeed it does exist at all, in regard to weight changes in the optic lens of the rabbit must be smaller than 362 rad. Calculation of the regression function of lens weight on rad dose results in the following formula:

$$\text{Lens weight} = (362.0 \pm 7.22) - (0.1166 \pm 0.0064)\,(\text{Dosage} - 1056\ \text{rad})\ \text{mg}.$$

The characterizing variances of this regression in Diagram 4 are given as the 'critical distance', *i. e.* they are an expression of the actual range of evidence supplied by the sample. The critical distance $\left(D_K = \frac{t_i \cdot s}{\sqrt{N}}\right)$ on a confidential basis corresponds to that distance from the mean value beyond which, at a preselected level of probability, any difference would be regarded as significant. For Diagram 4 the confidence limit has been chosen with $i = 0.05$.

The same procedure has been applied to illustrate the actual range of evidence of the means for the single dose groups in Diagram 5. The D_K's for the regression mean and the regression coefficient as well as for the mean values for the single dose groups have therefore been inserted. The area confidentially covering the 'true' regression may be expected to possess the smallest amount of variation at the sample mean of the dose values since the maximal or minimal regression coefficients have to be inserted radiating from this point in both directions. The control values at zero dose have been disregarded in calculating the regression formula. The mean of the control values does not differ in a significant way from the mean regression line interpolated to zero.

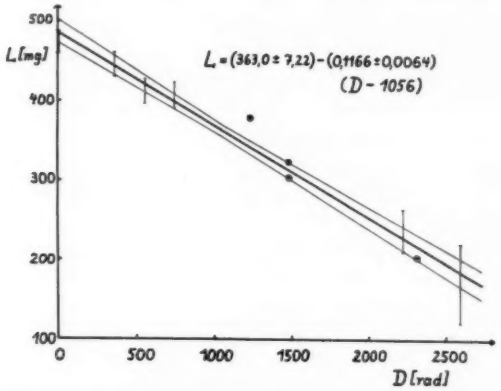


Diagram 5. Linear regression phase of lens weight on the dose of irradiation. The range of variations for the mean of regression and regression coefficient, as well as for the single dose groups observed, is indicated as the critical distance.

Discussion

In biologic irradiation experiments, more than with any other experiments, the date of irradiation and that of registering the effect have to be considered in the light of the existing relationship of these data to the duration of life of the subject of investigation (Diagram 1). The analysis of the irradiation damage on rabbit eyes — especially of weight changes in the optic lens — has shown that these time relations exert a decisive influence on the dose-effect relation.

The assumption of the existence of similar conditions in other biologic subjects seems obvious. This means that any results, for example on the relative biologic effectiveness of different radiation qualities on the irradiation sensitivity of different living subjects, can bear only limited validity. The existence of a linear dose-effect relation could be shown for the first time for a somatic radiation damage within a certain range of doses and as nearly as possible be demonstrated as a true one. The statistical analyses, furthermore, provide evidence that probably the dose-effect regression proceeds in a linear way to zero. As this linear dose-effect regression in later stages develops into a sigmoid relationship, the possibility has to be considered that with changes in the rate $t_1/t_2/t_{total}$ some radiation effects may escape observation.

For this reason the concept of the 'indifferent dose' (HOLTHUSEN) for biologic effects with sigmoid dose-effect relations has to be re-examined. The approximately linear dose-effect regression thought to be charac-

teristic for genetic radiation damage may be understood by the peculiar time relation of genetic experimentation. The variable t_2 in such experiments is confronted with a t_3 that can be regarded as infinitely large for practical calculation. The interval t_1 in this case represents an undetermined variable as it cannot be regarded as identical with the age of the experimental animal at the time of irradiation. On the contrary, t_{total} is always a finite entity in somatic radiation damage. The intervals t_1 and t_2 are related by a variable, notwithstanding a definite proportion to t_3. The independency of the always uniform and approximately linear dose-effect regression of genetic damages on the age of the experimental animals and on the length of t_2 chosen, is explained by these greatly different time relations.

The varying dose dependency found with somatic radiation effects cannot be interpreted in terms of the classical theory of hits (Trefferntheorie). Instead, the influence of the degree of vitality suggests a hypothesis according to which the respective biologic states of the irradiated subjects influence the form of the dose-effect relation observed. In the light of present knowledge it cannot be decided if this influence of the vital state involves regenerative processes. It seems, however, of practical importance to recognize that even in mature lenses, when growth processes have come to an end, some reactivity to irradiation exists and that this mature reactivity obeys the systematic reaction patterns found in animals of all ages.

SUMMARY

Weight changes in the optic lens of the rabbit caused by somatic radiation damage are described and discussed as demonstrating a variability of the dose-effect regression.

ZUSAMMENFASSUNG

Die bei somatischen Strahlenschaden verursachten Gewichtsänderungen der Augenlinse in Kaninchen sind untersucht worden und ein wechselhaftes Verhalten der Dosiseffektbeziehung wurde nachgewiesen.

RÉSUMÉ

Les auteurs décrivent les modifications du poids du cristallin du lapin sous l'effect de radiolésions somatiques; elles montrent que l'effet et la dose ne sont pas dans un rapport constant.

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FROM SAINT LUKE'S HOSPITAL (MEDICAL DIRECTOR: OLIVER CHANCE), DUBLIN IRELAND

INTEGRAL DOSE IN MOVING-BEAM IRRADIATION

by

Fearghus O'Foghludha

Few studies have been reported of the total absorbed energy or 'integral dose' in a body exposed to a moving beam of radiation, though there are many methods of estimating the dose at any point in such a body. A knowledge of the integral dose would be valuable in comparing different geometries and beam energies but the usual procedures for estimating it require that the complete dose distribution be known. The following develops another method, mentioned briefly elsewhere (O'FOGHLUDHA 1956), which can be applied up to HVL 15 mm Cu, at least, if the irradiated body is homogeneous and the radiation source revolves fully or partially about a line parallel with the body axis. The method is applied in examples to circumaxial and excentric rotation about cylinders.

The integral dose in a right circular cylinder is easily found if the cylinder and rotation axes are coincident and normal to the plane of rotation. The total energy absorption is then the same as if a stationary beam was used to deliver the given axis-dose, for the total surface dose, to which the integral dose is proportional, is the same whether the beam is moving or stationary, though the surface doses at a chosen point may be different in the two cases. To obtain the integral dose per D_x roentgens at the axis of a cylinder with radius x, it is then necessary to perform only a single-field calculation for a plane-parallel slab of thickness $2x$ in which a dose D_x is delivered at depth x. Any method which includes the effect of scattered radiation may be used for this calculation and the

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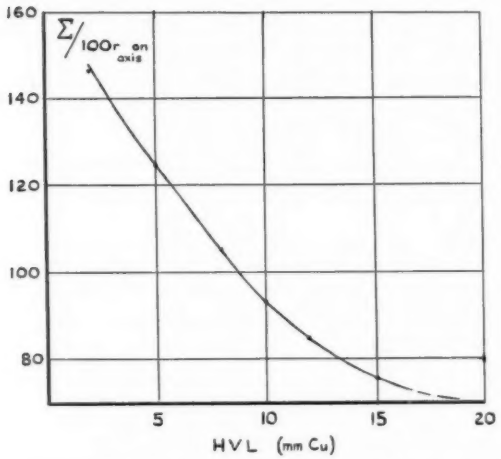

Diagram 1. Variation with HVL of the integral dose (in kg-r) per 100 r at the axis of a 12 cm radius water-equivalent cylinder. The field size is 20 cm² at the centre of rotation and the rotation radius is 112 cm.

dependence of integral dose on cylinder radius and other variables can be examined using single-field data only.

The quality dependence is easily investigated in this way, and Diagram 1 shows the variation of integral dose (from now on written Σ) with HVL. The ordinates were calculated by a method discussed later and represent the integral dose per 100 r at the axis of a water-equivalent cylinder with radius 12 cm. The rotation radius is 112 cm in all cases and the field area at the centre of rotation is 20 cm². The expected decrease in Σ with increasing HVL is observed, but the curve falls less steeply at higher energies and it is clear that raising the energy indefinitely offers little advantage as far as integral dose is concerned, a view supported by calculating Σ at 22 MeV in the same geometry, using the method and data of JOHNS and co-workers (1950).

In constructing Diagram 1 the rotation radius R is kept constant. The result might be different if the comparison were based on the rotation radius giving the greatest percentage depth dose at each energy; the field-size, of course, is fixed by the tumour dimensions and is not at the operator's disposal. The difficulty in choosing the best rotation radius lies in the well-known fact that the percentage depth dose increases continuously with R (WACHSMANN and BARTH 1953) and has no maximum at any usable radius, suggesting that R should be as large as possible if intensity is not important. An optimum value R_{opt} can, however, be de ined as follows:

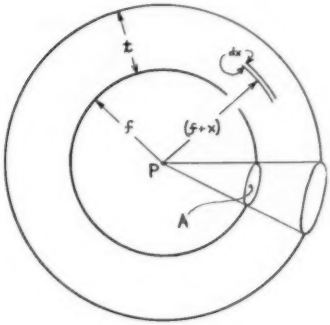

Diagram 2. Scheme employed in calculating integral dose.

The rotational percentage depth dose at fixed R is greatest at a certain cylinder radius r_m whose value depends on R. R_{opt} is that R for which r_m is the same as the body radius, and at R_{opt} the beam is most advantageously used as far as depth dose is concerned. For if R is less than R_{opt} the percentage depth dose is also less, while at greater radius R' the percentage depth dose, though larger than at R_{opt}, is less than the maximum which could be obtained at R' by using a cylinder of different diameter. A numerical study using R_{opt} at each energy and a suitable solid angle at each R_{opt} reveals, however, that the concept of optimum radius is of limited value, since variations in the factors of which Σ per unit axis dose is composed conspire to make it a slowly-varying function of R.

The integral doses per unit axis dose are the same for moving and stationary fields only in the symmetrical geometry postulated above. In practical radiotherapy the irradiated body is seldom of circular cross-section nor is the centre of rotation usually on the body axis. The FSD, the field area on the skin and the depth of the rotation centre therefore change as the source rotates, and only the source-strength and the solid angle of the beam are constant. To investigate the effect of these variations on Σ we need to know how the integral dose in a plane-parallel slab of fixed thickness depends on the FSD when the slab is exposed to a normally-incident beam of fixed solid angle.

From the expression of JOHNS and co-workers (1950) giving the integral dose at 22 MeV in terms of FSD, one can deduce that Σ at fixed thickness and solid angle is for all practical purposes independent of FSD at that energy, and a similar expression must hold for all energies high enough to ensure the virtual absence of sideways scatter. BRUCKMOOSER and KELLER (1956) have endeavoured to show that Σ is also independent of FSD at energies where lateral scatter is appreciable; though their calculations, using a modified form of WACHSMANN's (1941) method underestimate the effect of scattered radiation, the present more detailed study bears out the correctness of their statement.

The following reasonably accurate method of calculating Σ (used in constructing Diagram 1) is valid at all energies and is employed here in preference to the more accurate procedures of HAPPEY (1941) and MEREDITH and NEARY (1948) because numerical integration is unnecessary and

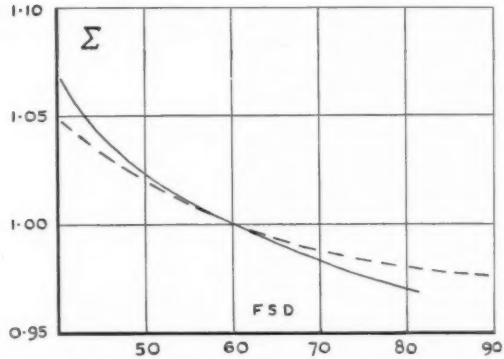

Diagram 3. Variation with FSD of integral dose per unit time in a beam of fixed solid angle (beam area 20 cm² at 50 cm from the source). The integral doses are normalized to unity at 60 cm FSD. Full line: HVL 1.5 mm Cu; broken line: HVL 15 mm Cu.

only one empirical constant needs to be known at each energy and FSD. It will be recognised as a combination of HAPPEY's 'saturated-pencil' concept and MAYNEORD's (1940) original method neglecting scatter. At HVL 1.5 mm Cu the answers given by it are roughly 10 % less than the true values and at higher energies the discrepancies are somewhat less.

Imagine a point source P at the centre of a spherical shell t cm thick (Diagram 2). When the shell is thick enough to absorb all the radiation emitted by the source, the integral dose per unit time is independent of the inner radius f (corresponding with the FSD). At smaller values of t absorption is incomplete and Σ must then be found by multiplying the local dose D_x at radius $(f + x)$ by the volume $4\pi(f + x)^2\,dx$ of an elementary shell at that radius, and integrating over the whole shell volume:

$$\Sigma = 4\pi \int_0^t D_x\,(f + x)^2\,dx \qquad (1)$$

By symmetry, the integral dose from radiation which falls on a limited area A cm² of the inner surface is $A/4\pi f^2$ times the energy absorbed in the whole shell. But this latter quantity is given by (1) and the integral dose in a shell segment of surface area A cm² can therefore be found. For the FSD's and field areas used in rotation therapy, such a segment is effectively a plane-parallel slab of thickness d, exposed to a collimated beam with surface area A cm². If we evaluate (1) and multiply by $A/4\pi f^2$ we can therefore calculate the integral dose in a plane-parallel slab at any f and so find the f-dependence of Σ.

Now D_x can to a good approximation be written $D_0 exp\,(-\mu x)$ where μ is MAYNEORD's (1940) apparent linear absorption coefficient; the value of μ, appropriate to a very large

field, is the one required in the sequel, since the uncollimated field of Diagram 2 is, in effect, infinitely large. The dose D_∞ cm on the inner surface can be written:

$$D_\infty = k_\infty P \qquad (2)$$

where k_∞ is the (saturation) surface backscatter factor for a very large field. Substituting in formula (1) and carrying out the integration, we obtain, for P primary roentgens on the surface

$$\Sigma = k_\infty PA\left[\frac{(1-e^{-\mu d})}{\mu}\left(1+\frac{2}{f\mu}+\frac{2}{f^2\mu^2}\right)-e^{-\mu d}\left(\frac{2d}{f\mu}+\frac{d^2}{f^2\mu}+\frac{2d}{f^2\mu^2}\right)\right] \qquad (3)$$

This expression contains only one f-dependent quantity μ, since k_∞ is fixed (PARKER 1935) and the product PA is made constant by the inverse-square law. Percentage depth dose tables for large areas show that μ varies very slowly with FSD — actually as $a-bf^{-1}$, where a and b depend on the energy and solid angle and have values that ensure slow variation — in the range of HVL already dealt with. It follows that Σ is to a very good approximation independent of the FSD (Diagram 3), and this result combined with JOHNS' work at higher energies allows us to conclude that Σ per unit time to fixed depth in a beam of constant solid angle is independent, over the entire therapeutic energy-range, of small variations in FSD such as occur in rotation therapy.

It is assumed that the block of tissue extends far enough sideways to ensure that all radiation scattered outside the beam is absorbed, but not far enough to render the surface noticeably curved. To check this point calculations were made by MEREDITH and NEARY's method, which alone of the standard procedures gives Σ in a volume outside the beam; the calculations show that in the usual rotation-therapy geometries the surface adjoining the field does not depart appreciably from planarity in the distance needed to give complete absorption.

MAYNEORD's method, which is similar in form to (3) differs from it in predicting a substantial increase in Σ with FSD. Now MAYNEORD's expression gives, as he clearly states, only the energy absorbed within the beam itself and therefore uses $\mu(A)$ rather the μ of (3), $\mu(A)$ being the value of μ for a beam of surface area A cm^2. Calculations by MEREDITH and NEARY's method show that the quantity given by MAYNEORD's expression becomes a larger fraction of the total energy-loss, which we have seen to be constant, as the field size increases. But the field size increases with FSD at constant solid angle and the f-dependence predicted by MAYNEORD's method is thus explained.

Though Σ is independent of f we cannot assume that it is unaffected by variations in FSD during rotation about an irregular contour, for changes in f alter the dose-rate at the tumour and with it the total time necessary to deliver a certain tumour dose. It is therefore no longer possible, as in the symmetrical case previously dealt with, to calculate Σ per unit axis dose without first performing a full rotational calculation of the tumour dose. It is nevertheless a great simplification to know that

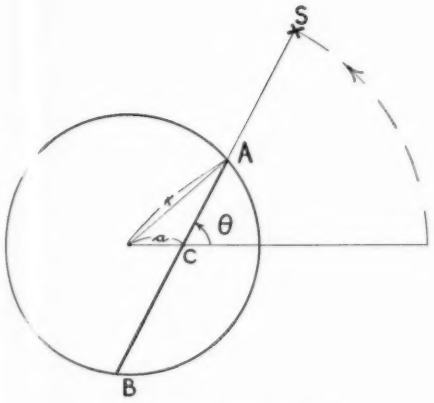

Diagram 4. (See the text below.)

variations in f need be considered in finding the tumour dose only and can be neglected in calculating the integral dose per unit time.

Assuming that small variations in FSD have little effect on the integral dose per unit time, we must now consider the second factor which could influence it, that is the variable thickness of tissue presented to the beam during rotation of the source. Simple contours only, such as circles or ellipses can be dealt with, but these represent human body-sections quite successfully. First Σ is found as a function of body-thickness t and this function is integrated around the chosen body-section. It turns out that the function giving the t-dependence of Σ is similar to that used by HAYNES and FROESE (1957) to represent the tumour-air ratio as a function of depth, but the elegant method of these authors for integrating their function about approximately elliptical contours has not been used in the present problem, for it loses much of its convenience when partial rotations or non-central tumours are dealt with. The method now described is more tedious than HAYNES and FROESE's for full, but less so for arc irradiations. It demonstrates the effects of off-centring the rotation axis in circular bodies and has the merit that the calculations can be used with slight modification to study the effect of eccentricity in the body-section itself.

To illustrate, first consider excentric rotation about a circular cylinder of radius r. Let the centre of rotation C (Diagram 4) be at a distance a from the axis and let $AB = t(\Theta)$ be the beam-length within the body when the source has moved through an angle Θ; the initial line is the radius through the centre of rotation but a simple extension of the method allows arbitrary choice of starting point. We require the average value $\overline{\Sigma_t}$ of the integral dose per unit time during a rotation from O to Θ, that is:

$$\overline{\Sigma_t} = \frac{1}{\Theta}\int_0^{\Theta} \Sigma_t \, d\Theta \qquad (4)$$

where we have written Σ_t for the integral dose per unit time at angle Θ and body thickness $t(\Theta)$. The integral can be evaluated by noting the empirical relation, valid in the HVL range 1.5 to 15 mm Cu:

$$\Sigma_t = \Sigma_\infty (1 - e^{-\lambda t}) \qquad (5)$$

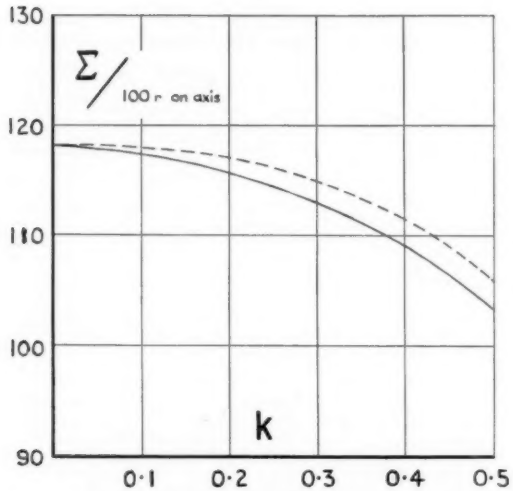

Diagram 5. Integral dose (in kg-r) per 100 r on rotation axis for a 12 cm diameter water-equivalent cylinder, plotted as a function of k, the degree of off-centering of the rotation axis. The HVL is 15 mm Cu and the field size 25 cm² at 75 cm rotation radius.

which can be verified by means of (3); here $\Sigma\infty$ is the integral dose in a very thick body at the chosen geometry, energy and source-strength, Σ_t is the integral dose to depth t under the same conditions and λ depends on the beam-energy only. Relation (5) is improved at small t by using two exponentials rather than one but at the thicknesses encountered in practical therapy the improvement is slight and has been neglected here, though it can be taken account of easily. Now $t(\Theta)$ is a known fuction of Θ:

$$t(\Theta) = 2r\sqrt{1-k^2\sin^2\Theta};\ k = a/r \tag{6}$$

where k is the eccentricity of the rotation centre. If we substitute the approximation (7),

$$t(\Theta) \simeq 2r\left(1-\frac{k^2}{2}\sin^2\Theta\right) \tag{7}$$

which is extremely good for $k \leqslant {}^1/_2$, into (5) and (4), we obtain

$$\overline{\Sigma_t} = \Sigma\infty\,(1-Fe^{-\lambda d}) \tag{8}$$

where $d = 2r$ is the cylinder diameter and F is the integral

$$F = \frac{1}{\Theta}\int_0^{\Theta} e^{\lambda r k^2 \sin^2\Theta}\,d\Theta \tag{9}$$

must be evaluated numerically, though if the interval of integration is a multiple of $\pi/2$, a case to which we shall confine ourselves, the calculations need be made in one quadrant only, for reasons of symmetry. F can be thought of as an eccentricity correction factor and is related to Δ the fractional reduction in integral dose per revolution brought about by off-centring the rotation axis, thus:

$$\Delta = \frac{(F-1)e^{-\lambda d}}{(1-e^{-\lambda d})} \tag{10}$$

For λ is less than 0.05 at HVL 1.5 mm Cu and decreases as the energy rises and in practice r never exceeds 20 cm, so that the case $\lambda r = 1$ gives the upper limit of the correction factors likely to occur in cylinders approximating to the human body. In this extreme case F is less than 1.05 up to $k = 0.3$ and one may therefore assume, if desired, that the integral dose in full revolutions is independent of eccentricity, to a first approximation. This approximation is not employed in what follows.

To find, next, the integral dose per unit axis dose we can employ HAYNES and FROESE's expression:

$$R = A_1 e^{-\alpha_1 x} - A_2 e^{-\alpha_2 x} \tag{11}$$

which relates the tumour-air ratio R with tumour depth x, at constant source-tumour distance. The average value $\bar{R}$ of the tumour-air ratio during a rotation can be determined since x is again a known function of Θ:

$$x = [r\sqrt{1-k^2 sin^2\Theta} - a cos\Theta] \tag{12}$$

Combining (12) and (11) and using approximation (7), we obtain for full rotation, if the small second term of (11) is neglected:

$$\bar{R} = \frac{A_1 e^{-\alpha_1 r}}{\pi} \int_0^{\pi} [exp\ \lambda r(k cos\Theta + \frac{k^2}{2} sin^2\Theta)]\, d\Theta \tag{13}$$

the interval of integration in this case being π, because of sign changes. When Σ as given by (8) is divided by (13), the integral dose for any axis dose delivered in a whole number of revolutions can be calculated. Diagram 5 shows how the integral dose per 100 r axis dose, in a circular cylinder of 12 cm radius, varies with the degree of off-centring of the rotation axis, at rotation radius 75 cm and a field size of 25 cm² at the axis. The HVL is 15 mm Cu, corresponding with cobalt 60 radiation. In these circumstances $A_1 = 1.21$ and $\alpha_1 = 0.0645$, according to HAYNES and FROESE, while $\lambda = 0.0309$.

For elliptical cross-sections the integrations are very laborious unless the centre of rotation is at either the centre or a focus. For the central case we obtain:

$$\left.\begin{aligned} \bar{\Sigma}_1 &= \Sigma \infty (1-Ge^{-2b\gamma}) \\ \bar{R} &= A_1 e^{-\alpha_1 b} \cdot H \end{aligned}\right\} \tag{14}$$

where G and H are the integrals

$$\left.\begin{aligned} G &= \frac{2}{\pi} \int_0^{\pi/2} e^{-b\lambda^2 sin^2\Theta}\, d\Theta \\ H &= \frac{2}{\pi} \int_0^{\pi/2} e^{-\frac{ab\lambda^2}{2} sin^2\Theta}\, d\Theta \end{aligned}\right\} \tag{15}$$

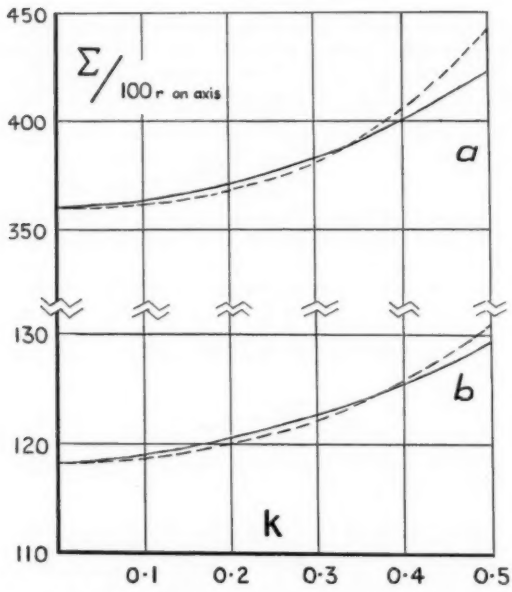

Diagram 6. Σ in kg-r per 100 r at the rotation centre (which coincides with the centre of the ellipse) in a water-equivalent ellipse of eccentricity k. Curve a refers to HVL 1.5 mm Cu and curve b to HVL 15 mm Cu. The minor semi-axis of the ellipse is 12 cm long and the field size is 25 cm² at 75 cm rotation radius.

Here b is the minor semi-axis and k is the eccentricity of the ellipse (*not* of the rotation centre), that is

$$k^2 = (a^2 - b^2)/a^2$$

where a is the major semi-axis. The terms needed to evaluate (G) are the reciprocals of those used in calculating (9), if the same energy, field-size and source-tumour distance are used, and b takes the place of r; the integral H can be evaluated similarly. The integral doses per unit axis dose can now be calculated as before and Diagram 6 gives Σ per 100 r axis dose as a function of body eccentricity at HVL's 1.5 and 15 mm Cu, for an ellipse with minor semi-axis 12 cm. The source-tumour distance is 75 cm in both cases and the field area at the centre of rotation is 25 cm², as before.

Similar calculations using some of the terms already evaluated can be carried out when the centre of rotation is at a focus. The only other case which lends itself to reasonably easy treatment (centre of rotation at a vertex) is of no practical interest. If the rotation centre is at some other point the computations become very tedious; in such cases, assuming that the centre of rotation is at a distance d from the ellips

centre and not necessarily on an axis, an approximate result can be obtained by noting that the answer must lie between that for eccentricity $k_1 = d/b$ in a circle of radius b, and that for eccentricity $k_2 = d/a$ in a circle of radius a, both of which cases can be treated by the method given. For partial rotations in both circular and elliptical sections, all that is required is to limit the range of integration accordingly, an operation that reduces the labour with little loss of accuracy, if the terms used in calculating the full rotations are also used for the smaller arcs.

The present calculations are not flexible enough for routine use, unless they are expressed graphically in terms of the parameters $b\lambda$ and ar. Their main advantage is rather that they serve as a criterion by which the success of less tedious approximations can be assessed. There is, in fact, one such approximation which renders the calculation of integral dose extremely easy. If the arguments rather than the functions (5) and (11). are averaged over the contour and the functions are evaluated at the averaged arguments, the answers differ negligibly from those given by the full methods. This is illustrated by the broken lines in Diagrams 5 and 6, which represent the results obtained by using the averaged thicknesses and radii vectors. In no case do the results differ by more than 3 % from those obtained by performing the complete calculations, and the results for partial rotations are equally good. The required average thicknesses and radii for circular and elliptical contours can be obtained with the help of tables of the elliptic integrals of the second and first kinds, respectively, and in irregular contours they can be measured with a ruler in a few moments.

The calculations take no account of body inhomogeneity, nor do they seem capable of modification to include this case.

Experimental work to check the calculations is in progress.

SUMMARY

The variation of integral dose per unit axis dose with HVL is discussed for circumaxial rotation about homogeneous cylinders. It is shown that the integral dose per unit time to fixed depth in a beam of fixed solid angle is independent of FSD over a wide energy-range. Using this fact and an empirical relation for the variation of integral dose with body thickness, the integral dose per unit axis dose is determined for excentric rotation about circular cylinders and for circumaxial rotation about elliptical bodies. A simple method for approximate calculation is discussed.

ZUSAMMENFASSUNG

Die Variation der Integraldosis per Zentralachsendosiseinheit mit der Halbwertschicht wird für die circumaxiale Rotation um homogene Zylinder herum diskutiert. Es wird gezeigt, dass die Integraldosis per Zeiteinheit für fixierte Tiefen in einem Strahlen-

bündel mit festgelegten Raumwinkel in einem ausgedehnten Energiebezirk vom Fokus-Hautabstand unabhängig ist. Bei Anwendung dieser Tatsache sowie einer empirische Beziehung der Variation der Integraldosis zu der Körperdicke wird die Integraldos per Zentralachsendosiseinheit für exzentrische Rotation um zirkuläre Zylinder heru und für circumaxiale Rotation um ellipsenförmige Körper herum bestimmt. Eine ei fache Methode für die approximative Berechnung wird diskutiert.

RÉSUMÉ

L'auteur étudie la variation de la dose intégrale par unité de dose axiale en fonctio de la CDA (HVL) dans le cas de la rotation périaxiale autour de cylindres homogène Il montre que la dose intégrale par unité de temps à une profondeur donnée dans u faisceau d'angle solide donné est indépendante de la DFP (FSD) dans un grand intervall d'énergie. Utilisant ce fait et une relation empirique reliant la variation de la dose inté grale à l'épaisseur du corps, l'auteur calcule la dose intégrale par dose axiale unité pou une rotation excentrique autour de cylindres circulaires et pour la rotation périaxiale autour de corps elliptiques. Il étudie une méthode simple pour le calcul approché de cett dose.

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BOOK REVIEWS

THE HAZARDS TO MAN OF NUCLEAR AND ALLIED RADIATIONS. Issued by the Medical Research Council. H. M. Stationery Office, London 1956. 128 pp. 5s. 6d.

THE BIOLOGICAL EFFECTS OF ATOMIC RADIATION. Summary Reports, and a Report to the Public. Issued by the National Academy of Sciences and the National Research Council, Washington 1956. 108 and 40 pp. resp.

EFFECT OF RADIATION ON HUMAN HEREDITY. Issued by the World Health Organization, Geneva 1957. 168 pp. $ 4.

RADIATION. WHAT IT IS AND HOW IT AFFECTS YOU. By Jack Schubert and Ralph E. Lapp. Viking Press, New York 1958. 314 pp. $ 1.25.

These five small books can well be reviewed together for though in some respects very different they have a common theme, and an important one, the radiation hazards of modern life. Until quite recently these hazards had been thought to concern only a limited section of the community consisting of those engaged in medical roentgenology and a few people using roentgen rays or radioactive substances in industry. With rapid development of nuclear energy and nuclear weapon-techniques, however, these hazards have risen enormously and, if allowed to get out of control, might wipe out the human race and all higher life from the earth's surface. The closer scrutiny of radiation effects prompted by these prospects have shown the hazards encountered in medical roentgenology and radioactivity work to be by no means as insignificant as has hitherto been commonly supposed, especially as these procedures are rapidly increasing. These books should be a challenge to the medical profession to do its best to avoid all unnecessary irradiation and thus play its part in the efforts to control the general radiation level. Roentgenologists, in particular, should try to convince their colleagues in surgery, medicine, gynecology, etc., that there are hazards not lightly to be dismissed and that some thought must be given to them before a patient is referred for roentgenologic examination or radiotherapy, especially if the lesion is benign, or the patient young.

The first-mentioned book gives, after an introductory chapter, a relatively brief but very useful account of the various genetic and somatic effects of radiation. The former effects are especially important for the whole population and might be very serious if the average dose due to artificial radiation were allowed to increase much above that due to the natural radiation. On the other hand, the hazards to direct descendants of individuals who have received larger doses, but still within the occupational level (60 r in the first 30 years of life), seem to be negligible. The level of natural radiation and of artificial radiation from different sources are reviewed. At present the most important source is diagnostic roentgenology which, according to a limited survey, contributes about 22 % of the natural radiation to the genetically effective dose (calculated with respect to the future child expectancy of the various patient groups). The American reports cited below give a figure of 70 %. In the long run, world-wide contamination from fission products such as Sr^{90} may produce still higher doses. Several important points are more fully explained in the appendices.

The American reports partly cover the same ground but also include chapters on meteorology, oceanography and fisheries, etc. from the point of view of radioactive contamination. The Summary Reports are condensed from fuller committee reports, of which only the one on oceanography and fisheries has been seen by the reviewer. Judging from its standard the full reports on genetics, pathology, and agriculture and food supplies, should be of a great interest to the readers of this journal. The 'Report to the Public' is even shorter and less technical, but certainly useful for its purpose. It is doubtful, however, if it has been possible in the limited space available (20 % of which contains committee membership lists!) to strike the right balance of warning the public without scaring it unduly.

In the W. H. O. report which has previously formed the subject of a review in Acta Radiologica (Vol. 49, p. 326), the genetic hazards are dealt with in more detail and the various natural and artificial sources discussed from this point of view by experts. The importance of the genetic aspects is well borne out, though most authors simultaneously stress the difficulties of arriving at tolerably reliable figures from the information now available. Desirable lines of biological and statistical research are sketched. A questionable point is the recommendation to record radiation exposure from medical and other sources of all members of a population. If available with any degree of accuracy and completeness, such information would certainly be extremely useful, but the possibility of obtaining it without prohibitive cost in medical and clerical work seems remote.

While stressing mainly the same points as the books reviewed above (largely the result of committee work), the volume by SCHUBERT and LAPP has a more personal character in expressing freely the opinions and apprehensions of the authors. In addition to popular accounts of the physical foundations and of various radiation effects, reports on a large number of radiation injuries due to accidents, ignorance, neglect, and sheer profit-making are included. There are unfortunately certain numerical errors, *e. g.* on p. 129, which result in a gross exaggeration of the hazards from iodine 131 and phosphorus 32. The extraordinary difficulties with waste disposal, safe as it must be even in the long run, from atomic energy work on a really large scale, and the extraordinary risks and hardships to be endured by the population in war with modern nuclear weapons are emphasized. The hazards in medical radiation work are much dwelt upon and patients are advised to question their doctors regarding the necessity for roentgenologic examination or treatment and on the doses to be given. However, a negative viewpoint is not unduly emphasized, but only unnecessary risk-taking is discouraged. It cannot be denied that too many doctors operating roentgen apparatus have insufficient knowledge of both radiation hazards and protection, as well as of the radiation output of their machines. This book should serve as a warning to them to remedy this shortcoming so that they can give their patients correct and complete information and dispel unfounded fear of radiation.

Sven Benner

EINFÜHRUNG IN DIE MESSTECHNIK DER KERNSTRAHLUNG UND DIE ANVENDUNG DER RADIOISOTOPE. Von Heinrich Fassbender. 223 S., 142 Abb. George Thieme Verlag, Stuttgart 1958. DM. 37: 50.

After a short and rather broad survey of the elements of atomic physics, the author describes different measuring methods and instruments; in most cases the type examples of the latter are German. Many illustrations, while technically good, consist of external views of instruments and have little informative value; basic diagrams are few in number and complete wiring diagrams are conspicuous by their absence. Nevertheless, the greatest value of the book to medical readers is contained in this chapter and in the concluding

ne on radiation protection. Applications of radioisotopes in medicine and biology are eated briefly as compared to their technical applications; as an extreme example, three ies are dedicated to intracavitary isotope therapy but twenty pages to the technicalities thickness gauges.

Sven Benner

NGIOCARDIOGRAPHIC OBSERVATIONS IN MITRAL DISEASE. By Håkan Arvidsson. 124 pages, 38 illustrations and 3 tables. Acta radiol. Suppl. 158 (1958). Sw. Kr. 30: —.

The object of this work was to investigate whether it is possible to make a differential diagnosis between various forms of mitral valve disease with the aid of angiocardiography. The method used was a slightly modified form of Jönsson's selective angiocardiography. The contrast medium was injected through a catheter into the main branch of the pulmonary artery and exposures made simultaneously in anteroposterior and lateral projections.

Technical equipment. An Elema biplane roll film changer capable of making six exposures per second was used. A Cournand catheter, size F 10 or F 12, with an end hole, was used in the majority of the cases. The contrast fluid was injected with a Gidlund pressure apparatus, which permits a high rate of injection. Simultaneous recording of electrocardiograms and exposures was arranged in order to ascertain in which heart phase the views had been obtained. The contrast medium used in most of the examinations was 60 % Urografin (Schering). With the exception of a few cases the examinations were carried out under insufflation anaesthesia. This was done both to spare the patient discomfort and to control the intrapulmonary pressure during the examination.

Clinical material. Seventy-three angiocardiographic examinations were made in 69 cases of mitral disease. Angiocardiography was thus carried out both before and after commissurotomy in 4 cases. A thorough cardiologic examination was performed prior to the angiocardiographic examination and pressure measurements in the right side of the heart with the catheter 'wedged' in a branch of the pulmonary artery were taken in conjunction with angiocardiography. The angiocardiographic diagnosis was verified in the 27 patients treated by surgery. The material was divided into three main groups according to the clinical and angiocardiographic observations, namely (1) pure mitral stenosis, (2) mitral stenosis and insufficiency, and (3) predominant mitral insufficiency. Each of these was subdivided into two groups, namely, cases with sinus rhythm and cases with fibrillation.

One of the essential aims of the investigation was to determine the volume and volume variations of the left atrium. After the theoretical aspects of this problem had been analyzed it was found that from the two projections of the atrium its volume could be approximately determined as an ellipsoid. By measuring the atrial volume in several different phases of the heart cycle it was possible both to determine the maximum volume variations and, in cases with regular sinus rhythm, to construct a curve showing the volume variations during the complete heart cycle.

The results of the volume measurements may be briefly summed up as follows. The smallest atrial volumes were observed among cases with pure mitral stenosis and predominant mitral insufficiency with sinus rhythm (means 145 and 155 cc), and the largest in cases with mitral insufficiency with fibrillation, and mitral stenosis and insufficiency with fibrillation (means 770 and 380 cc). The maximum volume variations were smallest in cases with mitral stenosis with fibrillation (mean 16 cc) and largest in mitral insufficiency with fibrillation (mean 125 cc).

The volume of the atrium could not be correlated either with the pulmonary artery

pressure or with the pressure measured with the catheter 'wedged' in a branch of the pulmonary artery. The volume curve for the left atrium during the heart cycle had different appearances in stenosis and in insufficiency with fibrillation; in stenosis, a slow evacuation of the atrium was observed in early diastole while a large part of the atrial evacuation took place at the atrial contraction; in insufficiency, very rapid evacuation took place in early diastole while the volume decrease was less marked during the atrial contraction.

The function of the left ventricle was also studied and an approximate determination of the ventricular volume in systole and diastole was also carried out in some cases. It was noted that the end systolic and end diastolic volumes of the left ventricle were influenced by mitral insufficiency and a complicating aortic valve disease. Aortic stenosis was often directly observed in lateral views in the form of thickened and rigid aortic valves, whereas it was not possible to obtain any direct evidence of aortic insufficiency.

In many cases the thickness of the left ventricular wall in diastole, and thus the degree of left ventricular hypertrophy, could be observed. In cases without left ventricular strain (pure mitral stenosis) the thickness of the wall varied between 7 and 10 mm.

The mitral valves and their movements were also observed. When a stenosis component was present in the mitral orifice, ballooning of the cusps in the left ventricle was noted during diastole owing to fusion of the apposition margins. In cases with mitral insufficiency, thickening and shortening of the leaflets was sometimes seen but no ballooning was observed in these cases.

From such observations it is possible, with the aid of this angiocardiographic method, to make a correct diagnosis in patients with valve defects in the left side of the heart. It may, however, be necessary in some cases to supplement the examination with an injection of contrast medium into the left ventricle or ascending aorta in order to obtain information regarding complicating aortic valve disease.

Autoreview

A Text-Book of X-Ray Diagnosis by British Authors. Vol. I. The head and the neck. Third edition. Edited by S. Cochrane Shanks and Peter Kerley. 521 pages, 538 illustrations. H. K. Lewis, London 1957. £ 4.10.

Not without irony and maybe some exaggeration it is often said that a new text-book is already antiquated when it appears in print. Few of the books which have recently been published can so justly warrant this criticism as the one now under review.

The greater part of the book deals with neuroradiology, the remainder covering the roentgen examination of the teeth and jaw, the nasal sinuses, the eye and ear, and the temporal bone. The chapter on the eye is devoted almost exclusively to the localization of foreign bodies while the diagnosis of intra-orbital expanding lesions receives hardly any attention at all.

The authors seem to possess little knowledge of new experiences gained during the last ten years or so; this applies to improvements in techniques in the pneumographic and other roentgen examinations as well. There consequently appears to be no point in entering upon a detailed discussion of the separate sections of the book. The editors in the preface state that enormous advances have been made in medical radiology since 1950 which makes it all the more regrettable that these have not been better reflected in the new edition. The inexactitudes are numerous and as so many of the recent advances and so much of our present knowledge in this field have been omitted the reviewer finds it hard to recommend the work. A clear and readable style should, however, perhaps be mentioned as one of its merits.

Torgny Greitz